S. HRG. 98-145

BIOMEDICAL RESEARCH, TRAINING, AND MEDICAL LIBRARY ASSISTANCE AMENDMENTS OF 1983

HEARING

BEFORE THE

COMMITTEE ON LABOR AND HUMAN RESOURCES UNITED STATES SENATE

NINETY-EIGHTH CONGRESS

FIRST SESSION

ON

S. 773

TO REVISE AND EXTEND PROGRAMS RELATING TO BIOMEDICAL RESEARCH, RESEARCH TRAINING, AND MEDICAL LIBRARY ASSISTANCE, TO ESTABLISH A NATIONAL INSTITUTE OF ARTHRITIS AND MUSCULOSKELETAL AND SKIN DISEASES, AND FOR OTHER PURPOSES

MARCH 17, 1983

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BIOMEDICAL RESEARCH, TRAINING, AND MEDICAL LIBRARY ASSISTANCE AMENDMENTS OF 1983

THURSDAY, MARCH 17, 1983

U.S. SENATE,
COMMITTEE ON LABOR AND HUMAN RESOURCES,
Washington, D.C.

The committee met, pursuant to notice, at 10 a.m., in room 4232, Dirksen Senate Office Building, Senator Orrin Hatch (chairman) presiding.

Present: Senator Hatch.

OPENING STATEMENT OF SENATOR HATCH

The **CHAIRMAN**. This morning we are meeting to consider legislation reauthorizing some of our most important Federal health efforts. The Biomedical Research, Training, and Medical Library Assistance Amendments of 1983 reauthorize the two largest Institutes at the National Institutes of Health—the National Cancer Institute and the National Heart, Lung, and Blood Institute. Also, the National Library of Medicine Assistance Act and the National Research Service Awards are reauthorized in this bill. The magnitude and the value of the activities encompassed in these programs are enormous. Together, they represent some of our Nation's most successful efforts to improve the health of our citizens.

The National Institutes of Health are unquestionably the premier biomedical research organization in the world. Research conducted by scientists funded by NIH has resulted in a tremendous expansion of our knowledge of disease and health. Fortunately, this knowledge has been translated into improved health for not only Americans but for people throughout the world.

I support our Government's commitment to biomedical research. This is a practical and proper role for the public sector. However, as an elected official, I have a duty to scrutinize closely this Federal presence, insuring that all tax dollars are spent efficiently and properly.

The legislation we are considering today preserves and continues the Federal Government's support for biomedical research and maintains the excellence of our National Institutes of Health. It reflects a vote of confidence in the scientists and administrators of NIH. They can be justifiably proud of their achievements, and we want them to continue their work with adequate funds to attract the best and brightest scientific minds to biomedical research. In order to maintain the momentum of our current research effort, I propose the authorization level be maintained at the significant increase appropriated in the continuing resolution for fiscal year 1983, and increase by 5 percent for fiscal year 1984 and by 5 percent per year thereafter. Although this level of funding applies only to the NCI, NHLBI, and the National Research Service Awards, I recommend similar increases for all of NIH.

During the course of these hearings, we will have an opportunity to hear of the recent accomplishments of NIH. But we will also address specific problems and concerns about our biomedical research efforts which have been conveyed to us by some citizens and professional organizations. Most common among these expressed are: (1) mismanagement of funds; (2) fraudulent research; (3) favoritism, resulting in funding primarily well-established research scientists; (4) resistance to funding research in unpopular or nontraditional therapies; and (5) overemphasis on biomolecular research at the expense of preventive and behavioral medicine research. I suppose there are others.

There is a legitimate basis for some of these allegations. However, I am doubtful that the way to solve these problems is by legislation. I prefer to convey the concerns of my colleagues and the citizens we represent to officials within HHS and NIH, with the full expectation that they will respond with efficient and effective solutions. In the 97th Congress, we introduced a biomedical research bill which made few changes in the authorizing statute, emphasizing the confidence we place in our current research effort. Nonetheless, we did require an annual report regarding activities to improve the grant, contracting, accountability, and peer review procedures at NIH. We also required the directors of specific research institutes notify the advisory boards of any investigation concerning a recipient of a grant or contract from NIH. Today, we will have an opportunity to learn of the progress made in addressing these issues.

The only significant change I am proposing in this legislation is establishment of a National Institute of Arthritis, Musculoskeletal, and Skin Diseases. I held full Labor and Human Resources Committee hearings devoted to this issue in July 1982. I am convinced that now is the time to focus a national effort to improve the prevention, diagnosis, and treatment of arthritis and, hopefully, to find cures to these painful and debilitating diseases. This new institute is necessary for this focus, given that these ailments are the most common and among the most costly of health problems afflicting our citizens.

At this point we will insert in the record the prepared statements of Senator Hawkins and Senator Dodd.

[The statements referred to follows:]

PREPARED STATEMENT OF SENATOR HAWKINS

Mr. Chairman, Although the legislation reauthorizing the National Institutes of Health, the National Cancer Institute and the National Heart, Lung and Blood Institute were not enacted last session, I don't believe that our efforts were in vain. I feel that the exercise was worthwhile because it afforded us an opportunity to review the programs and policies of the NIH. The biomedical research conducted by these Institutes cannot be measured in purely economic terms. The advances in medicine pioneered by the NIH have saved innumerable lives and enhanced the quality of life for millions of individuals. We can be justifiably proud of the work of these Institutes. But we can not afford to be complacent.

Despite the significant advances in research already achieved by NIH, this Institute still faces a formidable challenge in developing better detection, treatment, and cure for diseases affecting hundreds of millions of individuals. The basic discoveries already made in biochemistry, physiology, and medicine offer an opportunity of better health care and well-being for all Americans. But we are merely at the threshhold of major advances in biomedical research. In order to take full advantage of this opportunity and insure Americans of better health care, we must first insure that we have a sound management system to capture these opportunities.

We must insure the integrity of research conducted at NIH, to prevent future charges of fraud and unethical behavior. We must insure that information about the progress of NIH sponsored research is disseminated to local physicians and medical centers throughout the Nation. We must insure that patients participating in human clinical trials are fully informed of the risks associated with their medication and course of treatment. We must insure that any and all adverse reactions to experimental drugs or treatment be reported to NIH and quickly reported to all physicians using that form of therapy. We must insure the cooperation and coordination among the various Institutes to facilitate the exchange of research information.

The Senate Labor and Human Resources Committee indicated its concern about these subjects during hearings in the 97th Congress. I hope that the National Institutes of Health and the National Cancer Institute have made progress addressing these issues in the interim.

PREPARED STATEMENT OF SENATOR DODD

Scientific research and technological development are coming to be seen as playing an increasingly important role in meeting national needs. Programs for economic recovery, employment, health, education, environment, foreign trade, and national security all contain major elements dependent or predicated on vigorous growth of basic research and the application of new knowledge for technological development.

The Federal role in supporting and guiding the Nation's research and development enterprise is a crucial one. It is one that has, unfortunately, been allowed to languish in recent years. As a source of R&D funds, the Federal contribution actually shrank from 65 percent of the total in 1965 to less than 50 percent in 1981. Since the 1960's overall Federal support for research and development has seen virtually zero growth (in constant dollars), with the exception of recently increased spending for military applications. As a proportion of the gross national product, national R&D expenditures have actually fallen at the same time that other industralized countries, such as West Germany, the U.S.S.R., and Japan, have shown strong growth. These disturbing trends will need to be reversed if the Nation's scientific and technological skills are to be relied on to meet future national needs.

While support for research and development has deteriorated in recent years, the core of the country's scientific and technological establishment has remained strong. In fact, recent developments in electronics, communications, and computer technology, the burgeoning of biotechnology and related biomedical fields, and new thrusts in plant and agricultural sciences suggest that the Nation stands at the threshold of major advances and opportunities to meet human needs.

Can these exciting developments lead to improvement in the national economy and assist with meeting challenges in other areas of the national interest? This will depend, in large measure, on support in the Congress for continuing research and applied technology. The future of the Nation's scientific enterprise will also depend on the development, at the national level, of wise public policies to address issues affecting the direction, conduct, and ultimate application of scientific research.

The CHAIRMAN. Today, we have three distinguished panels. First of all, we will hear from the administration, represented by Dr. Edward Brandt, the Assistant Secretary for Health. He will be accompanied by the Director of the National Institutes of Health, Dr. James Wyngaarden, and directors of three of the research institutes and the Director of the National Library of Medicine.

We also have a distinguished science panel here today, including Dr. Timothy Talbot, the former Director of the Fox-Chase Cancer Center, Dr: Samuel Fox III, a cardiologist at Georgetown University, and Dr. Ephraim Engleman, a prominent specialist in rheumatology from the University of California. I am particularly pleased that Dr. John Dixon, from my home State of Utah, is also on this panel. He is the only physician I know who has served as both dean of the College of Medicine and the president of the Utah State Medical Association.

Finally, I am pleased that Dr. Chase Peterson is here, representing the Association of American Universities and higher education. Dr. Peterson is the vice president for health science at the University of Utah, and I might add a close personal friend, and I believe does as good a job in his particular office as any person in this country. I think he is a person we should well listen to.

With that, we will turn to our first panel. I am pleased to welcome representatives of the administration here today. The testimony, as I understand it, will be provided by you, Dr. Brandt, as Assistant Secretary for Health and Human Services.

Dr. Brandt has had the pleasure and pain of appearing before this committee several times over the past few years. He is accompanied by a distinguished group of physician scientists who have risen to positions of prominence and leadership in their profession. I am pleased to welcome Dr. James Wyngaarden, Director of the National Institutes of Health; Dr. Vincent DeVita, Director of the National Cancer Institute; Dr. Claude Lenfant, Director of the National Heart, Lung, and Blood Institute; Dr. Lester Salans, Director of the National Institute of Arthritis, Diabetes, and Digestive and Kidney Diseases; Dr. Martin Cummings, Director of the National Library of Medicine; and Dr. William Raub, Associate Director for Extramural Research and Training at NIH.

I understand Dr. Brandt will be offering oral testimony for the administration, and these distinguished gentlemen will be available for questions from the committee relative to their responsibilities. Dr. Brandt, we will turn the time over to you.

I am going to apologize, but with my severed achilles tendon, I am going to put my right leg up on the desk here. So I hope you will not feel that as an insult.

Dr. **Brandt**. Indeed, Mr. Chairman, I think all of us would agree that it is medically indicated that you keep that leg elevated.

The **Chairman**. Some of your people in your shop down there, I think, have enjoyed my walking around with a cane and crutches.

STATEMENT OF DR. EDWARD M. BRANDT, JR., ASSISTANT SECRETARY FOR HEALTH, U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES, ACCOMPANIED BY DR. JAMES WYNGAARDEN, DIRECTOR, NATIONAL INSTITUTES OF HEALTH; DR. VINCENT T. DeVITA, JR., DIRECTOR, NATIONAL CANCER INSTITUTE; DR. CLAUDE LENFANT, DIRECTOR, NATIONAL HEART, LUNG, AND BLOOD INSTITUTE; DR. LESTER SALANS, DIRECTOR, NATIONAL INSTITUTE OF ARTHRITIS, DIABETES, DIGESTIVE AND KIDNEY DISEASES; AND DR. MARTIN CUMMINGS, DIRECTOR, NATIONAL LIBRARY OF MEDICINE, A PANEL

Dr. **Brandt**. I do appreciate this opportunity to testify in support of the reauthorization of several vital components of the National Institutes of Health.

As you pointed out, I am accompanied by appropriate persons from the NIH, so we can respond to your questions and try to provide the kind of information that this committee needs to make its decisions. I would like to request that statements that have been prepared by the Directors of the National Heart, Lung, and Blood Institute; the National Cancer Institute; the National Institute of Arthritis, Diabetes, and Digestive and Kidney Diseases, and the National Library of Medicine be included as a part of the record of this hearing.

The CHAIRMAN. Without objection, we will include them as part of the record.

Dr. BRANDT. At the outset, Mr. Chairman, let me express on behalf of the administration and on behalf of all of us concerned with the health and well-being of people, appreciation for the concern and support that you and members of this committee have extended to the National Institutes of Health and its programs. We are speaking of more than an agency; we are talking about a national research enterprise that embraces the entire health sciences community—the Federal Government, academia, industry, and the philanthropic and voluntary sectors. All have important roles to play in the conquest of disease and disability, an effort, I am pleased to say, in which we are making great progress.

Progress grows out of the objectives embodied in the mission of the National Institutes of Health: the search for fundamental knowledge, the support and training of investigators who provide continuity in the research endeavor, and the timely dissemination of knowledge for public health and patient care.

Section 301 of the Public Health Service Act continues to provide a broad charter for the conduct of biomedical research. It offers the flexibility which enables NIH to take advantage of emerging scientific opportunities and to respond to changing health needs. This law, which illustrates the foresight of Congress, has served the Nation well.

The bill which you introduced last week, Mr. Chairman, carries forward that flexibility. While we have some reservations and concerns, as I will point out, in principle we support its objectives, and we believe they are consistent with the goals of the administration.

As you know, Mr. Chairman, authorizations for appropriations for several vital NIH programs expired at the end of fiscal year 1982, and those programs are now operating under the 1983 continuing resolution. To provide continuity in these programs, we have transmitted to the Congress legislation which would provide 5-year reauthorizations at the President's budget level for fiscal year 1984 and at such sums as may be necessary for fiscal years 1985 through 1988, for the following: expiring programs of the National Cancer Institute [NCI], the National Heart, Lung, and Blood Institute [NHLBI], and the National Library of Medicine [NLM]; the National Research Service awards program; and the National Institute of Arthritis, Diabetes, and Digestive and Kidney Diseases' [NIADDK's] Diabetes Research and Training Centers and Diabetes Data System and Information Clearinghouse, National Arthritis Advisory Board, National Diabetes Advisory Board, National Digestive Diseases Advisory Board, arthritis data system, and Multipurpose Arthritis Centers.

In addition, we have no objection to the provisions in your legislation, Mr. Chairman, relating to investigation of alleged scientific misconduct and the creation of an appeals procedure for grant applicants. In fact, Mr. Chairman, the Public Health Service, with NIH as the lead agency, has already started to develop a systematic approach to real or apparent scientific misconduct. I recently approved a set of policy statements and recommendation of the Public Health Service task force addressing these issues, and we will shortly be issuing guidelines to the agencies and awarding institutions in this area.

Let me now turn to two other provisions of S. 773, one that would require a study of the organizational structure of NIH and another that would establish a National Institute of Arthritis, Musculoskeletal, and Skin Diseases. We agree with the need to conduct a study of the NIH organization, but regretfully, Mr. Chairman, we do not support your proposal for a new arthritis institute. I do believe, however, that there is room for accommodation that will satisfy the concerns we all share in these matters for people who suffer from those illnesses.

In an appearance before this committee last year, Dr. Wyngaarden expressed some views concerning the structure of NIH that are still timely today. He pointed out that modern biomedical research focuses increasingly on the underlying processes of sickness and health and less so on the symptoms of specific disease entities. He suggested that the current stage in the development of biomedical knowledge and of NIH make this an appropriate time to take a close, analytical look at the structure of the research endeavor and its management. We are, indeed, faced with the question of whether organizational complexity tends to be counterproductive.

Because of those concerns, we have negotiated a study that I believe will be responsive to your objectives, Mr. Chairman. We have negotiated and are in the process of completing our negotiations with the Institute of Medicine of the National Academy of Sciences for a comprehensive 18-month evaluation of the organization of NIH. We have asked them to conduct a thorough, systematic review of NIH's organizational evolution and development and to examine the present structure of NIH and its underlying rationale. We have asked them to examine NIH's present approach to those issues which cut across organizational lines and to develop alternative approaches for consideration and finally, in light of scientific developments and economic conditions, to develop rationale and criteria upon which to base future changes.

From this summary, Mr. Chairman, I think you can see that the study that you have proposed in S. 773 would go far beyond the one that we have negotiated and would require the collection of more data and more detailed analyses than are necessary to address the central issues before us. We believe the study we have proposed, Mr. Chairman, would focus more directly on the fundamental organizational questions we face.

I should note that in recent years, there have been 10 proposals for new institutes and 5 proposals to transfer to NIH functions from other Public Health Service agencies. We therefore agree with you, Mr. Chairman, that a moratorium should be imposed on the creation of new institutes. We suggest, however, that this moratorium continue until the results of the IOM study have been reviewed appropriately. We also recommend that the moratorium include a ban on the transfer of other components to NIH during the same interim period. We must, however, disagree with the proposal that an exception to this moratorium be made to allow creation of an arthritis institute.

In the interim, I can assure you, there will be no relaxation of the NIH effort to pursue understanding of arthritis and related diseases that afflict so many people. The NIADDK, recently elevated to a bureau of the Public Health Service, conducts and supports highly effective and comprehensive programs of basic and clinical research and training related to arthritis and musculoskeletal and skin diseases. In fact, over the period 1976–82, the arthritis division has been the fastest growing in that institute and one of the most rapidly expanding programs thoughout NIH.

To underscore my belief that significant advances have been made in arthritis research, I would like to submit for the record a summary of research accomplishments, together with a list of major initiatives undertaken or planned by the NIADDK to enhance research efforts related to arthritis, musculoskeletal, and skin diseases.

Let me also express my concern that the additional administrative costs of establishing and operating a new institute would seriously erode the funds available for research essential to continued progress. I will also submit for the record, Mr. Chairman, an analysis that places the startup and initial operating costs of a new institute at $4.8 million. Expenditure of that sum translates into a reduction of 25 to 30 percent of the funds available to support new and competing grants for research into arthritis and musculoskeletal and skin diseases.

I hope, Mr. Chairman, that you and members of your committee will agree that the information gathered by the IOM study will help us make sound decisions in the long run regarding the structure of NIH and its programs, and that a temporary delay in a decision on the establishment of an arthritis institute will in no way diminish the vigor with which answers to that malady are being sought under the existing institute and its programs.

My colleagues and I will be pleased to answer questions Mr. Chairman.

[The prepared statement of Dr. Brandt follows:]

STATEMENT BY EDWARD N. BRANDT, JR., M.D.

Mr. Chairman and Members of the Committee:

I appreciate this opportunity to testify in support of the reauthorization of several vital components of the National Institutes of Health (NIH). With me today is Dr. James B. Wyngaarden, Director of NIH.

Also present to respond to questions are: Dr. William F. Raub, NIH Associate Director for Extramural Research and Training; Dr. Vincent DeVita, Director of the National Cancer Institute (NCI); Dr. Claude Lenfant, Director of the National Heart, Lung, and Blood Institute (NHLBI); Dr. Lester Salans, Director of the National Institute of Arthritis, Diabetes, and Digestive and Kidney Diseases (NIADDK); and Dr. Martin Cummings, Director of the National Library of Medicine (NLM). I request that statements prepared by the Directors of NCI, NHLBI, NIADDK and NLM be included as part of the record of today's hearing.

At the outset, Mr. Chairman, I want to express, on behalf of the Administration and all of us concerned with the health and well-being of people everywhere, appreciation for the concern and support you and members of this Committee have extended to NIH and its programs. We are speaking of more than an agency; we are talking about a national research enterprise that embraces the entire health sciences community--the Federal Government, academia, industry, and the philanthropic and voluntary sectors. All have important roles to play in the conquest of disease and disability, an effort in which we are making great progress.

The multi-billion-dollar public investment by the Congress over the past 30 years has built a national capacity for innovative biomedical and behavioral research unmatched by any other nation or society. This is an area in which the Federal Government has played--and should continue to play--a leadership role. Our diverse, nationwide biomedical research enterprise is writing an extraordinary chapter in the annals of world medicine. I want to reaffirm today that this Administration shares with Congress a strong commitment to the strength and continued growth of our effort to understand and overcome disease and disability. Progress in this area grows out of the objectives embodied in the mission of NIH: the search for fundamental knowledge, the support and training of investigators who provide continuity in the research endeavor, and the timely dissemination of knowledge for public health and patient care.

Congress underscored its faith in the value of health research decades ago, when it consolidated and revised laws relating to the Public Health Service in 1944. Section 301 of the PHS Act continues to provide a broad charter for the conduct of biomedical research. It offers the flexibility which enables NIH to take advantage of emerging scientific opportunities and to respond to changing health needs. The law, which illustrates the foresight of Congress, has served the Nation well. As science and public need evolve, it has been necessary through the years to mount specific efforts under the general authority of the PHS Act; the inherent flexibility of the law has permitted those activities.

The bill you introduced last week, Mr. Chairman, carries forward that flexibility. While we have some reservations and concerns, in principle we support its objectives and believe they are consistent with the goals of the Administration. The legislation provides for continuity in the Nation's research enterprise while at the same time acknowledging the need for conservative fiscal management of all Federal programs.

As you know, Mr. Chairman, authorizations for appropriations for several vital NIH programs expired at the end of Fiscal Year 1982, and those programs are now operating under the 1983 Continuing Resolution. All of these programs contribute to progress in the understanding, treatment, and prevention of disease. Through timely dissemination of research findings to other investigators and to medical care practitioners, they make the benefits of that knowledge available to the public. To provide continuity in those programs, we have transmitted to the Congress legislation which would provide five-year reauthorizations at the President's budget level for Fiscal Year 1984 and at such sums as may be necessary for Fiscal Years 1985 through 1988 for the following:

o Expiring programs of the National Cancer Institute; the National Heart, Lung, and Blood Institute; and the National Library of Medicine;

o The National Research Service Awards program; and

- NIADDK's Diabetes Research and Training Centers and Diabetes Data System and Information Clearinghouse; National Arthritis Advisory Board; National Diabetes Advisory Board; National Digestive Diseases Advisory Board; arthritis data system; and multipurpose arthritis centers.

I request that the Administration bill I have described be included as part of the record of this hearing. You will note, Mr. Chairman, that our proposal includes a number of provisions that are not contained in S.773. We hope that the Committee will give consideration to these provisions during its deliberations on your bill.

We have no objection to the provisions in your legislation relating to investigation of alleged scientific misconduct and to creation of an appeals procedure for grant applicants. In fact, Mr. Chairman, the Public Health Service (PHS), with NIH as lead agency, has already started to develop a systematic approach to real or apparent scientific misconduct. This includes a description of the responsibilities of both awardee institutions and PHS staff, as well as detailed procedures governing PHS activities before, during, and after formal investigations. I recently approved a set of policy statements and recommendations of the PHS task force along these lines, and we will shortly be issuing guidelines to the agencies and awardee institutions in this area.

I would like to turn now to two other provisions of S.773--one that would require a study of the organizational structure of NIH and another that would establish a National Institute of Arthritis and Musculoskeletal and Skin Diseases. We agree with the need to conduct a study of NIH organization, but regretfully, Mr. Chairman, we oppose your proposal for a new arthritis institute. I believe, however, that there is room for accommodation here that would satisfy the concerns we share in these matters.

In an appearance before this Committee last year, Dr. Wyngaarden expressed some views concerning the structure of NIH that are still timely today. He pointed out that modern biomedical research focuses increasingly on the underlying processes of sickness and health, less so on the symptoms of specific disease entities. Given the many still unsolved disease entities, he noted, there is virtually no end to the possibilities for creation of additional categorical institutes. He suggested that the current stage in the development of biomedical knowledge, and of NIH, makes this an appropriate time to take a close analytical look at the structure of the research endeavor and its management. From both fiscal and managerial points of view, we are faced with the question of whether organizational complexity tends to be counterproductive in science, management, and economics.

Because of those concerns, we have negotiated a study that, I believe, will be responsive to your objectives, Mr. Chairman. We have negotiated with the Institute of Medicine (IOM) of the National Academy of Sciences a comprehensive, 18-month evaluation of the organization of NIH. We have asked the IOM to:

- Conduct a thorough and systematic review of NIH's organizational evolution and development and to examine the present structure of NIH and its underlying rationale;

- o Examine NIH's present approach to those issues which cut across organizational lines and develop alternative approaches for consideration; and,

- o In light of scientific developments and economic conditions, develop rationale and criteria upon which to base future changes.

From this summary, Mr. Chairman, you can see that the study you have proposed in S. 773 would go far beyond the one we have negotiated and would require the collection of more data and more detailed analyses than are necessary to address the central issues before us. For example, your bill calls for the development of standards for realigning combinations of disease research programs in each of the Institutes; a study of the effectiveness of the existing combinations of disease research programs within the Institutes; and a study of the effectiveness of the organization and administrative structures of each of the Institutes, including the effectiveness of the advisory councils, advisory boards, and interagency committees that carry out functions relating to each Institute.

We believe the study we have proposed, Mr. Chairman, would focus more directly on the fundamental organizational questions we face and enable us to respond in a rational way to repeated pressures for additional institutes and other components at NIH. I should note that in recent years there have been ten proposals for new institutes and five proposals to transfer to NIH functions from other PHS agencies. We therefore agree, Mr. Chairman, that a moratorium should be imposed on the creation of new institutes. We suggest, however, that this moratorium continue until the results of the IOM study have been reviewed appropriately. We also recommend that the moratorium include a ban on the transfer of other components to NIH during the same interim period.

We disagree with the proposal that an exception to this moratorium be made to allow creation of an arthritis institute.

We respectfully suggest, Mr. Chairman, that such an exception runs counter to the careful approach taken in your proposal for an IOM study. Extension of a moratorium to the establishment of any new institute would reflect not a lack of commitment to progress in arthritis-related research, but a real commitment to finding the best possible approach to that goal and to continued excellence throughout all of the NIH programs.

In the interim, I can assure you, that there would be no relaxation of the NIH effort to pursue understanding of arthritis and related diseases that afflict so many people. The NIADDK, recently elevated to a bureau of the PHS, conducts and supports highly effective and comprehensive programs of basic and clinical research and training related to arthritis and musculoskeletal and skin diseases. In fact, the arthritis program area is the fastest growing program in that Institute and one of the most rapidly expanding programs throughout NIH.

To underscore my belief that significant advances have been made in arthritis research, I have attached to my statement a summary of research accomplishments, together with a list of major initiatives undertaken or planned by the NIADDK to enhance research efforts in arthritis, musculoskeletal, and skin diseases (Attachments A-D). I also want to express my concern that the additional administrative costs of establishing and operating a new institute would seriously erode the funds available for research essential to continued progress in this area. I have also attached to my statement, Mr. Chairman, an analysis that places the startup and initial operating costs of a new institute at upward of $4 million (Attachment E). Expenditure of that sum translates into a reduction by 25 to 30% in the funds available to support new and competing grants for research into arthritis, musculoskeletal and skin diseases.

I hope, Mr. Chairman, that you and members of the Committee will agree that the information gathered by the IOM study will help us make sound decisions in the long run regarding the structure of NIH and its programs. And, that a temporary delay in a decision on the establishment of an arthritis institute will in no way diminish the vigor with which answers to that major health problem are being sought under the existing institute and its programs.

I will be pleased to answer any questions you may have.

TAB A

NIH RESEARCH ADVANCES IN ARTHRITIS

- A Possible Cause of Rheumatoid Arthritis (NCI and NIADDK)
- New Method for Treating Rheumatoid Arthritis (NCI and NIADDK)
- A Potential New Approach to Drug Therapy for Rheumatoid Arthritis
- Genetic Determinants in Juvenile Arthritis
- Biomedical Studies of Osteoarthritis (NIA and NIADDK)
- Discovery of Factor that Causes Inflammation of Joints in Gout and Pseudogout
- Purinogenic Immunodeficiency Diseases (Metabolic Diseases, NIADDK)
- Lyme Arthritis (NIAID and NIADDK)
- Advances in Joint Replacement (Musculoskeletal Diseases, NIADDK)
- Viral Gene Product Immune Complexes in Experimental Systemic Lupus Erythematosus (SLE) (NIAID)
- Sex Hormone Abnormalities in Systemic Lupus Erythematosus
- High Blood Levels of Interferon in Lupus (SLE) (NCI and NIADDK)
- Plasmapheresis in Lupus Nephritis (Kidney Diseases, NIADDK)
- New Monoclonal Antibody Technique May Prove Useful in Treatment of Lupus (SLE)
- Life-Saving Treatment for Scleroderma Kidney Disease (NHLBI and NIADDK)
- New Blood Antibody Test as a Marker for Mild Form of Scleroderma
- Life-Saving Treatment for Wegener's Granulomatosus (NIAID)
- Fluoride Therapy of Osteoporosis (Musculoskeletal Diseases, NIADDK)

A Possible Cause of Rheumatoid Arthritis

Several NIADDK-supported investigators (Drs. Vaughan, Tan, Alspaugh, Zvaifler et al) have reported high levels of serum antibodies to Epstein-Barr (EB) virus in patients with rheumatoid arthritis. EB virus is the cause of both infectious mononucleosis and a special form of cancer, Burkitt's lymphoma. Most Americans have been "infected" with EB virus by early adult life. In normal individuals the virus has the capacity of eliciting antibodies to EB virus, but these are then eliminated by specialized white blood cells, the suppressor type of T-lymphocytes. Drs. Todaro and Blaese, intramural scientists at the National Cancer Institute (NCI), working in collaboration with Dr. Steinberg, an intramural scientist at NIADDK, have recently discovered and reported (NEJM, Nov. 1981) a specific defect of T-lymphocyte suppressor cells for EB virus in rheumatoid arthritis.

New Method for Treating Rheumatoid Arthritis

Radiation treatment of lymph glands and other lymphoid tissues, called "total lymphoid irradiation" or TLI, had been shown by extensive research supported by the National Cancer Institute (NCI) over several years to be highly effective, and reasonably safe, in the treatment of Hodgkin's disease and other lymphoid tumors. In that the efficacy of TLI seemed to be mediated by immunotherapeutic mechanisms, NIADDK-supported scientists reasoned that TLI therapy might be effective in treating non-malignant autoimmune diseases. Two recent feasibility studies, performed independently at the Harvard and Stanford Arthritis Centers, have shown striking reductions of joint inflammation, lasting for months, in patients with severe rheumatoid arthritis unresponsive to all other forms of treatment.

Of additional interest was that during the suppression of the arthritis, there was no reduction of serum autoantibodies, previously thought to be important in causing the arthritis. Rather, there were changes in white blood cell ratios, thus redirecting research emphasis towards the area of cell-mediated immunopathology.

This illustrates the applicability of research in one medical area, in this case, cancer, to another, arthritis, in terms of both treatment and cause.

A Potential New Approach to Drug Therapy for Rheumatoid Arthritis

Researchers at the Dartmouth Arthritis Center are investigating in tissue culture the effects of retinoic acid, a derivative of vitamin A, on joint lining cells from patients with rheumatoid arthritis. They have shown that retinoic acid both inhibits the production of collagenase, an enzyme which destroys joint cartilage, and also inhibits production of prostaglandin E-2, a fatty acid which fosters joint inflammation.

Genetic Determinants in Juvenile Arthritis

As many as 250,000 children in this country have one or another form of juvenile arthritis. What was once called "juvenile rheumatoid arthritis" is actually a group of several distinct disease states which differ according to joints involved, severity of arthritis, age of onset, and complications. Complications include skin rash, growth retardation and iritis (inflammation of the eyes possibly leading to blindness).

Dr. Peter Schur and colleagues in Boston have found an increased frequency of the genetic marker, HLA-DRW5, in children with the form of juvenile arthritis that carries a risk of iritis. HLA testing, therefore, may identify children with arthritis who are at risk for eye complications. In another study, Johns Hopkins investigators have found another marker, HLA-B27, in a special subset of juvenile arthritis, i.e. young women who develop in childhood a form of arthritis that initially resembles rheumatoid arthritis, but then progresses later to develop arthritis of the neck.

Biomedical Studies of Osteoarthritis

In research supported by NIA and NIADDK, Dr. Roland Moskowitz et al at Case Western Reserve University has developed an experimental animal model of osteoarthritis in rabbits to study biochemical and cellular changes in the development of this disease. Results suggest that onset of osteoarthritis is associated not with gross abnormalities in overall metabolism of proteins, nucleic acids, or polysaccharides, but rather deficiencies in specific complexes of proteins and polysaccharides. They have also shown that estrogens aggravate experimentally-induced osteoarthritis, and that tamoxifen, a drug with anti-estrogenic effects, appears to ameliorate the condition.

Discovery of Factor that Causes Inflammation of Joints in Gout and Pseudogout

A significant contribution has been made to knowledge of the pathogenesis of the acute highly inflammatory crystalline-induced arthritis of gout and pseudogout. Investigators at Washington University (Dr. Spilberg et al) have shown that when polymorphonuclear leucocytes (white blood cells) ingest either urate or calcium pyrophosphate crystals, they release a factor, called crystal chemotactic factor or CCF. This factor has been shown, when injected into rabbits, to induce an inflammation indistinguishable from that seen in the acute arthritis of gout or pseudogout.

Purinogenic Immunodeficiency Diseases

Specific abnormalities of purine metabolism, identified by research supported by the Metabolic Diseases Program of NIADDK, have been shown to be important, not only in gout, but also in the development of immunodeficiency states.

Lyme Arthritis

This new form of arthritis was discovered in 1976 by researchers at Yale University in three Connecticut coastal towns. In a series of productive epidemiologic and clinical investigations supported by NIADDK, the arthritis was found to be characterized by a distinctive antecedent skin rash (erythema chronica migrans), recurrent arthritis and, in some patients, late neurologic and cardiac complications; and to be transmitted by a tick, Ixodes dammini. Cases have since also been found in other parts of the country. Early penicillin treatment was then shown to reduce the incidence of the late complications. Scientists at the NIAID's Rocky Mountain laboratory have recently discovered (Science, June 10, 1982) the likely cause of the disease by both identifying treponemal spirochetes in the ticks and demonstrating anti-treponemal antibodies in the serum of patients with Lyme arthritis. This is an example of highly productive research sponsored by two different institutes leading to the discovery of both the cause and treatment of a new multisystem rheumatic disease.

Advances in Joint Replacement

Artificial joint replacement has been developing rapidly, with approximately 75,000 hip replacements and 40,000 knee replacements performed annually. Short-term success for these implants is now established. Long-term prognosis (10 years and beyond), however, is less certain, because of the tendency of the replacement to loosen with time.

Dr. Amstutz, a NIADDK-sponsored scientist at the University of California, Los Angeles, is studying fixation materials that would be alternatives to acrylic cement. Of various porous materials tested, bone growth into implants was fostered by sintered cobalt beads. Dr. Specter of the University of South Carolina has demonstrated good shear strength and early ingrowth of bone with porous plastic-coated prostheses. Dr. Von Recum at Clemson University in South Carolina, has shown that precoating the stem of the prosthesis with cement yields a simpler surgical procedure and improved strength.

Viral Gene Product Immune Complexes in Experimental Systemic Lupus Erythematosus (SLE)

With NIAID support, Dr. Frank Dixon of the Scripps Clinic and Research Foundation continues his pioneering studies of animal models in SLE. Studies of the mouse model have shown that a viral gene product, a major envelope glycoprotein called GP-70, appears to be selectively expressed in sera and in epithelial and lymphoid tissues. Circulating immune complexes that contain GP-70 have been associated with the development of fatal kidney disease, and conceivably could be used to predict the course of kidney disease in lupus patients by computing rising levels of serum GP-70 linked with antibodies.

Sex Hormone Abnormalities in Systemic Lupus Erythematosus

Systemic lupus erythematosus (SLE or lupus) is a potentially serious generalized autoimmune disease that attacks many parts of the body. Early on, there is arthritis and skin rash; it also affects other organs such as the kidneys, heart, or brain. Lupus primarily affects young women of childbearing age; the female to male ratio is 9:1.

Experimental animal models of lupus have been developed in inbred strains of New Zealand and other specially developed strains of mice.

Recent research has indicated the importance of sex hormones in the development of lupus. NIADDK grantee Dr. Norman Talal and colleagues demonstrated that estrogens (female hormones) accelerate and androgens (male hormones) suppress the development of SLE in experimental mice. Recently, Drs. Lahita and Kunkel of the Rockefeller University in New York reported that women with lupus have an abnormality of estrogen metabolism. This may explain, for the first time, the female predominance of SLE.

High Blood Levels of Interferon in Lupus (SLE)

High serum levels of alpha-interferon have been discovered in patients with SLE by Dr. Robert Friedman of the NCI, and related to intracellular inclusions by NIADDK scientists and to disease activity by scientists at University of Michigan (Dr. Thomas Schnitzer et al). Whether this interferon in SLE indicates a viral infection or serves as an immuno-regulator needs to be clarified.

Plasmapheresis in Lupus Nephritis

Several reports have indicated possible beneficial effects of plasmapheresis, a blood separating or "cleansing" technique, in lupus patients with severe kidney involvement, presumably by removing from the patients' blood immune complexes which are thought to be responsible for kidney injury in lupus. The Kidney Diseases Program, NIADDK, has recently awarded a grant to Dr. Edmund J. Lewis of Chicago for a multicenter (14 institutions) controlled study to determine the efficacy and risks of plasmapheresis in lupus nephritis.

New Monoclonal Antibody Technique May Prove Useful in Treatment of Lupus (SLE)

NIADDK grantee Dr. Bevra Hahn and her colleagues in St. Louis have found that anti-DNA antibodies, produced in large quantity by the new monoclonal antibody technique, given in early life, can prevent the emergence of lupus nephritis in New Zealand mice, an inbred strain that serves as an experimental model of lupus. When untreated, 60 percent of these mice die of kidney disease at 6-8 months of age. All mice injected with anti-DNA antibodies at 6 weeks of age were alive after 7 months of age. It is important to find the mechanism by which this increased survival occurs, so that these results might be applied to patients.

Life-Saving Treatment for Scleroderma Kidney Disease

New effective drugs (inhibitors of angiotension-converting enzymes--e.g., Captopril), developed with NHLBI support for the treatment of severe hypertension have proven life-saving in patients with scleroderma kidney disease, a fatal complication of this connective tissue disease. Coincident with the blood pressure reductions and preservation of kidney function, softening of hardened sclerodermatous skin and healing of finger ulcers have also been reported in some patients. NIADDK and NHLBI are planning collaborative support of research on the microcirculation in Raynaud's phenomenon and scleroderma.

New Blood Antibody Test as a Marker for Mild Form of Scleroderma

Patients with the limited CREST form of scleroderma have been discovered to have in their serum a specific autoantibody to the chromosomal centromere of cell nuclei. This provides physicians with a new laboratory test marker that indicates a favorable prognosis in certain patients with scleroderma.

Life-Saving Treatment for Wegener's Granulomatosus

NIAID intramural scientist, Dr. Fauci, and his colleagues have clearly established the extraordinary efficacy of the cytotoxic agent, cyclophosphamide, in treating patients with this previously highly fatal systemic vasculitic disease.

Fluoride Therapy of Osteoporosis

Osteoporosis is a common important disease characterized by reduced bone mass and increased susceptibility to bone fractures, particularly in older women. Most forms of treatment, including estrogen replacement, act by retarding loss of bone mineral. Researchers have found that sodium fluoride plus calcium can stimulate bone formation. There is concern, however, about the strength of fluoride-induced bone and other reported side effects. NIADDK has initiated a collaborative clinical trial of fluoride-calcium in two institutions under the direction of Dr. Riggs at the Mayo Clinic and Dr. Kleerekoper at the Henry Ford Hospital in Detroit.

TAB B

National Institute of Arthritis, Diabetes, and Digestive and Kidney Diseases
Division of Arthritis, Musculoskeletal and Skin Diseases
Selected Program Accomplishments

Possible Cause of Rheumatoid Arthritis

Patients with rheumatoid arthritis have high levels of several antibodies for EB virus, the virus that causes infectious mononucleosis. Researchers have now discovered a specific defect in those cells (T-suppressor lymphocytes) that modulate antibody production to EB virus, thus providing an insight into the cause of rheumatoid arthritis.

New Approach to Treatment of Rheumatoid Arthritis

Total lymphoid irradiation, an established, highly effective treatment method for lymphoid cancers, has been shown to reduce joint inflammation in severe rheumatoid arthritis, refractory to all other forms of treatment, presumably by normalizing the ratio of T-suppressor lymphocytes to T-helper lymphocytes.

High Blood Levels of Interferon in Lupus (SLE)

High serum levels of alpha-interferon have been discovered in patients with lupus (SLE) and related to disease activity. Whether this interferon indicates a viral infection or serves as an immune regulator needs clarification.

New Monoclonal Antibody Technique in Treatment of Lupus (SLE)

Anti-DNA antibodies, produced by the new monoclonal antibody technique, given in early life, can prevent the emergence of lupus nephritis in New Zealand mice, an inbred strain that serves as an experimental model of lupus. This is a potential new approach to the treatment of systemic lupus erythematosus (SLE), a serious disease of young women.

New Blood Antibody Test as a Marker for Mild Form of Scleroderma

Patients with the limited CREST form of scleroderma have been discovered to have in their serum a specific autoantibody to the chromosomal centromere of cell nuclei, thus providing a laboratory test marker that indicates a favorable prognosis in certain patients with scleroderma.

Promising New Drugs to Treat Raynaud's Phenomenon

To counter the vasospasm (constriction of small blood vessels) of Raynaud's phenomenon that occurs as part of scleroderma or lupus, or by itself, encouraging results have been reported recently from preliminary therapeutic trials with Nifedipine, Prostacyclin and Captopril.

Cause and Treatment Found for New Form of Arthritis

The cause (Treponemal spirochete form of bacteria), method of transmission (by a tick), and treatment (penicillin) have all been discovered for Lyme arthritis, a disease first recognized only in 1975.

Improved Artificial Joints

Improvements of prosthetic design and biomaterials for artificial joint implantation have improved postoperative success rates, especially in total knee replacements recently.

Molecules Discovered That Cause Bones to Grow

Molecules that regulate and promote the growth of bone have now been isolated from animal and human bones. One of these, Bone Morphogenic Protein, has been reported to be dramatically useful in repairing bone defects in the heads of children. Human Skeletal Growth Factor, another such protein recently discovered, has been found to be elevated in the blood of patients with Paget's disease, a chronic disorder characterized by bone enlargement.

Defect in Collagen Formation in Osteogenesis Imperfecta

In the dominant form of osteogenesis imperfecta, a major inherited connective tissue disease that causes bones to fracture spontaneously, the Type I collagen of bone is reduced in amount, although chemically normal. Recent research has shown that this is due to a deficient production of the alpha-1 chain precursors of collagen. This finding has both etiologic and therapeutic potential.

Muscle Research to Improve Exercise Training

Recently obtained knowledge of basic muscle exercise physiology can foster the design of more efficient exercise training programs.

Effects of Mechanical Forces on Chemical Composition of Cartilage

Advances in both biomechanics and biochemistry of cartilage are providing new opportunities for determining their interrelationships and the mechanisms of joint destruction in osteoarthritis and traumatic arthritis.

Importance of Newly Discovered Cells in Allergic Skin Diseases

Langerhans cells, residing in the epidermis, have now been shown to serve as antigen-presenting cells and to be important in delayed hypersensitivity reactions in the skin. Corticosteroids inhibit these reactions by decreasing the number of Langerhans cells in the skin.

Anti-Convulsant Drug Helps Blistering Disease

The drug, diphenylhydantoin, has been shown to reduce significantly the incapacitating blistering of epidermolysis bullosa (EB), a serious genetic disorder of children.

Relatives of Vitamin A Effective in Acne and Scaling Skin Diseases

Retinoids, newly synthesized analogues of vitamin A, have proved effective in treating severe cystic acne, and appear highly promising in the treatment of serious scaling disorders of the skin such as psoriasis and the ichthyoses.

Autoantibodies Shown to Cause Blisters of Pemphigus

Immunoglobulins from the serum of patients with pemphigus vulgaris, a severe and at times fatal blistering disease affecting skin and mucous membranes, when administered to experimental mice, induces skin blisters and erosions identical to those seen in human pemphigus. This proves that the antibody is directly involved in causing the disease. It also elevates the importance of the antibody as an index of disease activity in monitoring the treatment of pemphigus. Further research is needed to discover how the antibody causes the blistering.

TAB C

A FRESH APPROACH TO ARTHRITIS AND MUSCULOSKELETAL DISEASES RESEARCH BY NIADDK

Recognizing the magnitude of the public health problem posed by arthritis and musculoskeletal diseases, and the many emerging scientific opportunities that now exist in these fields, the National Institute of Arthritis, Diabetes, Digestive and Kidney Diseases (NIADDK) is making a new and vigorous effort to intensify arthritis related research. Under the strong leadership provided by the new Director, Lester B. Salans, M.D., and the new NIH Director, James B. Wyngaarden, M.D., most of the previous problems impeding arthritis research programs at NIH are now being addressed and effectively resolved. Some actions already taken by Dr. Salans, as well as others to be initiated in 1983, follow.

MANAGEMENT INITIATIVES ALREADY UNDERTAKEN

Establishment of NIADDK as a Bureau and Creation of the Division of Arthritis, Musculoskeletal, and Skin Diseases

- Recent bureau status has helped NIADDK to achieve an increased level of visibility and strength within the NIH and the Department of HHS.

- Bureau status has enabled new NIADDK leadership to improve managerial effectiveness and enhance NIADDK relationships with its advisory and constituent groups. The Institute has initiated a comprehensive program of management initiatives which enhance greatly the strength and visibility of its arthritis and musculoskeletal diseases research programs.

Relationships with Health Care Voluntaries

- Improvement of working relationships with professional and lay groups having an interest in NIADDK, through meetings with representatives and elected members of all of NIADDK's major organizations. In February, Institute staff senior staff held a series of intensive meetings with members of the Arthritis Foundation, the Academy of Orthopedic Surgeons, and leading researchers in arthritis and musculoskeletal diseases, to discuss current problems and future strategies. On February 22, a second annual meeting was held between NIADDK management and all relevant health voluntary groups, including arthritis and orthopedics. A NIADDK COALITION HAS BEEN FORMED, THE FIRST OF ITS KIND AT NIH, TO ARTICULATE TO THE PUBLIC THE MANY EXCITING OPPORTUNITIES WHICH NOW EXIST AND THE NEED TO SUPPORT ALL AREAS OF NIADDK RESEARCH. That Coalition adapted and presented to the Congress a unified budget request for 1983.

- Increased NIADDK involvement with and support of the activities of the National Arthritis Advisory Board. The Chairman of the National Arthritis Advisory Board now regularly attends the meetings of the NIADDK National Advisory Council.

Relationships with Scientific Community

- Meetings of senior staff of NIADDK and leading researchers in arthritis and musculoskeletal diseases have been initiated on a regular basis.

- Regional meetings with NIADDK management and grantees of the Institute have been initiated in an effort to strengthen relationships with academia.

Internal Initiatives

- Development of a new system for allocating funds among the Institute's Divisions, with a view towards greater involvement of the Divisions in the budget process.
- Development of a new planning process for the Institute which provides, for the first time, an opportunity for the outside scientific and lay community to become involved in the Institute's planning and budget process.
- Stronger role for the Institute's Arthritis and Musculoskeletal Diseases Division Director in order to achieve greater independence and public visibility.
- Establishment of an Arthritis and Musculoskeletal Diseases Division Advisory Committee to interact with Institute staff, the Institute's National Advisory Council and the National Arthritis Advisory Board.
- Identification of research projects that cut across categorical disease areas and are common to more than one program, in order to more closely integrate and coordinate NIADDK support of related research, e.g., arthritis and endocrinology.

Within the current NIADDK organization close, strong and productive interrelationships exist among many of our categorical disease programs, with common threads of basic research underlying all of the Institute's disease areas. This is particularly so for arthritis research.

One of the many forms of arthritis is systemic lupus erythematosus (SLE). This disease affects many organs of the body. Lupus affects the kidney and is of special concern to the NIADDK Kidney program. Lupus affects the skin and is under study by the Skin Diseases program. The treatment of lupus with adrenal steroids is closely related to research in the Endocrinology program. Blood cell abnormalities in SLE are under investigation by scientists in the Hematology and Nutrition programs.

Like SLE, rheumatoid arthritis appears to have a genetic and immunologic basis. Genetic and immunologic abnormalities similarly lead to diabetes, certain forms of kidney and digestive diseases, and various endocrine disorders and metabolic diseases. Research supported by NIADDK in each of these categorical disease areas is following similar tracks with regard to presumed causative genetic and immunologic factors. Like arthritis, diabetes is a disease that disproportionately afflicts the aging population. Research into the factors responsible for this common characteristic is closely interrelated in this Institute. These kinds of collaborative efforts benefit from the research climate that now prevails in the NIADDK and the Institute is taking steps to strengthen this unique opportunity.

NEW NIADDK INITIATIVES IN ARTHRITIS AND MUSCULOSKELETAL DISEASES RESEARCH IN 1983

- New Research Initiative in Arthritis. Announcement soliciting applications for research on the etiology of rheumatoid arthritis.

- New Initiative in Musculoskeletal Disease Research. Announcement soliciting applications for research in an area to be identified through the Institute's current evaluation of this field, which will be completed in 1983.

- Two New Research Training Initiatives. Development of two specifically targeted new training awards in arthritis and musculoskeletal diseases: the Special Emphasis Research Career Award and the Physician Investigator Development Award.

- Establishment of the Trans-NIH Arthritis Research Program. NIADDK plans to discuss with the NIH Director the development of a trans-NIH arthritis program with lead responsibility in the Director of the Division of Arthritis and Musculoskeletal Diseases, NIADDK. This program would identify, encourage, and highlight arthritis and musculoskeletal diseases-related research in other NIH institutes. For examples, NIADDK and the National Institute on Aging share an interest in osteoarthritis and osteoporosis. Juvenile arthritis can be addressed by NIADDK and the National Institute of Child Health and Human Development. The immunologic basis of rheumatoid arthritis and SLE is of concern to both the NIADDK and the National Institute of Allergy and Infectious Diseases.

  NIADDK is making vigorous efforts to enhance cooperative initiatives in arthritis research among relevant NIH institutes and to promote a trans-NIH arthritis program.

CONCLUSION

The arthritis and musculoskeletal diseases programs of the NIADDK are strong and highly productive. With new vigorous, innovative and committed leadership, and continued public and congressional support, the Institute is making substantial progress towards addressing and responding to the needs of arthritis and musculoskeletal diseases research in an efficient and effective manner. We view the 1980's as a period of unprecedented scientific opportunity and accelerating research momentum. We are committed to taking full advantage of the many scientific leads in arthritis and musculoskeletal diseases, so that the benefit of NIADDK research can be effectively applied to improve the health of our citizens.

TAB D

ARTHRITIS PROMOTION PLAN

March - May 1983

The Office of Health Research Reports, NIADDK, is currently undertaking the following projects:

1. Publicizing the availability of the NIADDK pamphlet How to Cope with Arthritis to medical and science writers; consumer publications; Arthritis Foundation chapters.

2. Announcing the appointment of Dr. Lawrence E. Shulman as Director, Division of Arthritis, Musculoskeletal and Skin Diseases, to trade journals and newsletters (Rheumatology News, etc.) as well as the Foundation's National Arthritis News, American Rheumatism Association newsletter, Arthritis Foundation chapters.
   Note: The Foundation's annual government affairs meeting is 3/14/83.

3. Producing, through the News Branch, a special issue of NIH News and Features on arthritis research, which will be mailed in mid-March to:

   1400 science writers
   Arthritis Foundation chapters
   Lupus Foundation chapters
   Lupus Society chapters
   Key congressmen and senators
   Multipurpose Arthritis Center Directors
   National Arthritis Advisory Board members
   Arthritis Interagency Coordinating Committee members
   NIADDK Council
   NIADDK press list

   In addition, the Office of Health Research Reports, NIADDK, will get 5,000 copies.

4. Cosponsoring a Community Forum on Arthritis with the local Arthritis Foundation chapter on May 17, 1983. Dr. John Decker, Chief of NIADDK's Arthritis and Rheumatism Branch will be the main speaker. Renee Pouissant, a local television anchorwoman, may also be a participant.

5. When it is available, publicizing a new publication called Medicine for the Layman: Arthritis, currently in press. It is based on a lecture by Dr. Decker from the "Medicine for the Layman" series of lectures given each fall and sponsored by the NIH Clinical Center.

6. Working with the NIH Audiovisual Branch, arranging a 15-minute taped interview on arthritis with Dr. Shulman which will include the NIH role in arthritis research. The Audiovisual Branch places such interviews on a local radio station (WGMS) on Sunday mornings and on a Los Angeles radio station (KRLA) and distributes them via satellite and on records to radio stations across the country.

TAB E

ESTIMATED ADMINISTRATIVE COSTS FOR A NEW INSTITUTE AT THE NATIONAL INSTITUTES OF HEALTH*

(Amounts in Thousands)

An estimated $4-5 million in administrative costs would be required to establish a new institute. This estimate is comparable to the actual direct operations and program management costs incurred by two of the smaller institutes at NIH in Fiscal Year 1981.

Following is a cost breakdown:

Accounting Category	
Salaries & Expenses	$1,817
Travel	140
Transportation of Things	3
Rent, Communications and Utilities	385
Printing and Reproduction	150
Other Services (consultants, consultant services contracts, conferences, workshops, management studies and evaluations, data processing, renovations, equipment repair, assessments for program evaluations and NIH general expense fund)	1,180
Payment for Centrally Furnished Services	960
Supplies and Materials	70
Equipment	60
	$4,765

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*It should be noted that sixteen positions--representing $800,000--could be transferred from the National Institute of Arthritis, Diabetes, and Digestive and Kidney Diseases (NIADDK) to a new institute for arthritis, musculoskeletal and skin diseases. The net administrative costs of the new institute would therefore be approximately $4 million. Although it has been suggested that NIADDK could transfer more than $800,000 to a new institute, this would not be feasible. Currently, NIADDK has an extremely lean and efficient administrative apparatus, which requires only approximately four percent of the total Institute's budget. This efficiency reflects the fact that most NIADDK administrative services are provided centrally to the Institute's ten program areas, including support services such as personnel management, program analysis, financial management, and grants management. If NIADDK were required to transfer more than $800,000 to the new institute, the research efforts and administrative management functions of the remaining programs in the Institute would be adversely affected. Ultimately, however, the lost resources would have to be restored, and the replacement costs would be attributable to creating the new institute for arthritis, musculoskeletal and skin diseases.

The **Chairman**. Thank you, Dr. Brandt. Let me ask several questions of the administration regarding concerns we raised during the last Congress related to NIH. As you know, we conveyed these concerns in the committee report which accompanied S. 2311. In lieu of multiple questions, I would appreciate your providing just a brief written response to each section of the report relative to NIH. I think that would be helpful to the record.

Dr. **Brandt**. We will certainly supply that.

The **Chairman**. This would give the committee an update on the progress of the concerns that we listed last year.

I understand that the administration is generally supportive of S. 773, the biomedical research bill that we are considering here today. However, I am fully aware that the administration is not supportive of the proposed National Institute of Arthritis, Musculoskeletal, and Skin Diseases. You previously cited concerns about administrative costs and setting a precedent for the creation of multiple new institutes. I want to know for the record how you can justify those concerns when much of the expertise and resources for the proposed Institute are really already in place in the National Institute of Arthritis, Diabetes, and Digestive and Kidney Diseases.

We have requested in the statute a careful study of the NIH administrative structure before additional institutes are created. My question is, Why would you not go along with us, because I think it is going to pass in the Congress? The only worry we have is what will happen to it when it gets to the House, which is what we went through last year.

Dr. **Brandt**. I think the basis, Mr. Chairman, for our position is as follows. One, we fully agree with you on the need for additional research and more effective answers to the problems that are posed by the diseases afflicting connective tissue, joints, the musculoskeletal system and the skin. We believe that the management of the NIH totally needs a careful look. We currently have 16 bureaus, institutes, and divisions at the NIH, but modern medicine is now becoming more integrated rather than separated. We believe that the creation of any new Institute should be delayed until we can take a look at management and organizational principles for such a research enterprise.

The **Chairman**. I might mention that if we create a new Arthritis Institute—and I intend to see that we do, if we can—we intend to solve your problems and concerns by funding it adequately. But we think you have already the making of an Institute right there. You have done a lot of interesting things in the field of musculoskeletal and skin problems and arthritis problems. So we hope you will consider chatting with the administration and consider the fact that there is a real good consensus developing on the Hill for such an Institute.

I have to admit, I trailed behind on whether or not we should do that last year because of the administration's feelings, but I really have come to the conclusion that with the millions and millions of people who are afflicted, we really ought to elevate that to the status where I think those people feel that they have more help on the way and where they can resolve some of these problems. I hope you will continue to look at that, even though I do understand your position and I understand what you are saying here today.

I am going to submit additional written questions to you, Dr. Brandt, if I can. Let me turn to Dr. Wyngaarden.

Perhaps the single most important complaint, Dr. Wyngaarden, that we hear from the biomedical research community is the perception that there is little attraction and even less security for young scientists to pursue a career in biomedical research. We hear that the financial status of NIH is deteriorating, that support in constant dollars has gone down over the past several years, and that young investigators are discouraged because of the intense competition for NIH research funds. Apparently, even highly rated grant proposals frequently go unfunded because of what we perceive to be very fierce competition for them.

I understand this frustration, but given the economy and the evolving Federal role, it seems obvious to me that NIH has received and enjoyed remarkable support from this administration and stands out as a single Federal health effort that has received increased funding, and I intend to see that you get increased funding in the future, as well as this year. However, I think you know that I do not support unlimited Federal expenditures.

I understand that the actual number of grant applications funded has not decreased over the past several years but that the number of applications deemed worthy of funding has increased. It seems to me it simply reflects the success in training and increasing the number of young research scientists who are capable of submitting excellent grant proposals. Furthermore, is not this high-quality competition really a healthy sign in the biomedical research field?

Dr. WYNGAARDEN. Senator, we agree with the statements you have made. Certainly, I want to commend you and other members of the committee for the strong support that you have given to the NIH at a time when the economy is not flourishing generally. It has permitted us to continue to fund many excellent programs and to maintain a strong research portfolio. Over the last few years, we have shifted funds from other mechanisms in order to continue to fund what we consider to be a minimum number of meritorious proposals, in the range of about 5,000 new and competing grants per year. Your support has also permitted us to continue to fund a reasonable percentage of young investigators, first-time applicants. Approximately one-third of all the new and competing awards we fund each year are in the new category. Approximately half of those, in turn, are given to first-time applicants in the system. That has been true for some years. The percentage of all our awards awarded to first-time applicants is currently in the range of 10 to 12 percent, and that has been a fairly stable figure for the past decade.

The increased competition is a mixed blessing. It enables us to support the very highest quality research, but it also means that many good investigators are not supported. But in spite of that competition, we have, through the competitive peer review system, managed to provide entry into the system for a fairly stable number of new investigators. I think that message needs to be emphasized, that there is a very bright future in biomedical research for the young investigator.

The **Chairman**. Could you please advise us what the NIH is doing to address what has become regarded a startling and well-publicized health problem? I am talking about the Acquired Immune Deficiency Syndrome. I understand that although this often fatal problem is at present limited to only certain segments of our population, there is grave concern that it heralds a new set of infectious diseases which we presently are unable to treat effectively.

As you know, there have been several proposals to set aside NIH funds into an emergency trust, with the idea that a significant amount of money could be targeted for research on new, acute medical problems. Do you believe that this is necessary, or can NIH respond expediently and efficiently to new threats to our public health?

Dr. **Wyngaarden**. Yes, sir. We share your concern and the public concern about the AID syndrome. It is a devastating problem, growing in severity. It deserves vigorous attention from many agency sources. The syndrome was first called to the attention of CDC in the spring of 1981. Within a few months, we had admitted patients to the NIH Clinical Center for study, and two NIH-supported centers—one in Seattle and one in Chapel Hill—were actively involved in investigating this problem. Our commitment to it has grown steadily ever since.

I have a chronology prepared of the development of knowledge about this syndrome and of the development of the NIH and PHS response that I would like to submit for the record.

The **Chairman**. Without objection, we will be happy to put it in.

[The information referred to follows:]

DATE	STATUS OF AIDS	NIH ACTIVITIES 3/31/83
Spring 1981 March - April 1981	CDC first learned about AIDS (homosexuals with *pneumocystis carinni*, N.Y. and L.A., 5 cases).	5 cases of *pneumocystis carinii* reported to the CDC by NIH grantee at UCLA.
Summer 1981		
June 5, 1981	Cases identified in San Diego; surveillance task force set up at CDC.	
June, July 1981	Epidemiologists sent to 16 cities to look for cases; interviewed victims.	First AIDS patient admitted to NIH Warren Magnuson Clinical Center.
September 1981		The NCI sponsored a workshop on AIDS. Other AIDS presentations were made to the NCI Division of Cancer Treatment's Board of Scientific Counselors and to the National Cancer Advisory Board in the fall.
Fall 1981 October, November 1981	Task force administared questionnaires to homosexual community in hopes of finding link for disease.	NCI investigators conduct pilot study to evaluate effect of amyl nitrate use in healthy homosexual men; results show lower T-cell ratios in inhalent users, which suggests an immunological deficiency. NEI intramural scientists identify the presence of cytomegalovirus in the retina of an AIDS patient; comprehensive eye examination and care provided to all AIDS patients admitted to the Clinical Center.
	New phenomenon of lymphadenopathy identified. First cases of AIDS in Haitians (researchers identified Kaposi's sarcoma and pneumocystis from autopsy reports).	NIAID supported Sexually Transmitted Disease (STD) Center at Univ. of Washington began prospective study of homosexual men; STD Center at Univ. of N.C. began study of immune response in gay men exposed to CMV infection.
December 1981		UCLA study (5 cases of pneumocystis carinii - noted above) published in the *New England Journal of Medicine*.
Winter 1982		
January 1982	216 AIDS cases, 88 deaths	
February 1982	Hemophiliac first case (pneumocystis).	NCI contract to evaluate the effect of amyl nitrate exposure in mice; results suggest immunological effects.
Spring 1982		
April 1982	Investigators traced a case from one individual which was spread to nearly a dozen sexual contacts. Viral theory explored - CMV.	NCI researchers conduct field study to determine immunologic status of healthy homosexual men. NIH researchers participated in inter-agency meetings on AIDS. Intramural NIAID begin studies of immuno-regulatory defect in AIDS patients; studies of herpes virus isolates from AIDS patients; also studies of Epstein-Barr and CMV infections in AIDS patients. Development of NCI Request for Applications on AIDS - (RFA) (approximately $1.25 million).

DATE	STATUS OF AIDS	NIH ACTIVITIES
Summer 1982		NLM began compilation of an exhaustive bibliography on AIDS. Intramural NIAID researchers investigating possibility of parvo-like virus in AIDS patients. Committee to Coordinate Environmental and Related Programs convened meeting on AIDS (NIEHS participant) because of possible involvement of environmental agent. NIH working group on AIDS established with representatives from each institute and liaisons from CDC and FDA. NCI RFA issued (August).
Fall 1982 September 1982		NHLBI convened working group with CDC regarding transmission of AIDS through blood products; agreed to contributed $150,000 to CDC efforts to expand program on investigation of blood products. NCI supplemental funding of current grants to encourage AIDS research (approximately $165,000). Receipt of responses to NCI RFA (October). Intramural NIAID begins investigation of role of hepatitis in AIDS using chimpanzees already used in hepatitis studies - (virtually all AIDS patients have had hepatitis). Intramural NIAID attempts bone marrow transplantation to restore immune function in AIDS. NIAID decision to contribute funds to NCI RFA (approximately $750,000).
December 198		Special Review Committee convened by NCI to review response to RFA. NCI and NIAID begin development of second RFA on AIDS for anticipated funding in FY 1984 (RFA requests research on possible infectious agents). NCI study of stored plasma samples from hemophiliacs thought to have had AIDS - discovery of elevated interferon levels; 45 healthy hemophiliacs evaluated in field-studies - no significant increase found in interferon levels.

DATE	STATUS OF AIDS	NIH ACTIVITIES
Winter 1983		
January 1983	Representatives from blood banks meet with Federal officials on AIDS.	NIH scientists attend blood bank meeting.
		Cold Spring Harbor meeting.
		NHLBI reconvened working group with CDC to plan conference and to explore result of CDC blood research.
		Intramural NHLBI extended use of its chimpanzees for the study of AIDS-like disease.
		National Cancer Advisory Board action on responses to first RFA (4 proposals approved for funding; ($341,000); 8 deferred for site visits).
		Intramural NIAID notes increased incidence of antibody to B lymphocyte host specific Papovavirus in AIDS.
		NIAID in-house review of NCI RFA responses.
February 1983		Intramural NIAID initiates trial of gamma Interferon in treatment of AIDS.
		Intramural NIAID attempts to transmit etiological agent of AIDS to chimpanzees and other primates.
March 1983	1112 AIDS victims (418 deaths); children identified with AIDS for first time.	DRR sponsored one-day conference on comparative medical aspects of AIDS in primates and humans.
		NCI researchers to present data on the immunology of healthy homosexual men at AIDS symposium at New York University.
		NHLBI-CDC conference on blood products to be held.
		Nearly 50 AIDS patients enrolled in Clinical Center research studies as either in-house or ambulatory patients.
April 1983		NIAID to sponsor symposium at which investigators who have been successful in isolating a causative agent in diseases with previously unknown etiology will discuss their methodological approaches and consult AIDS investigators.

NIH ACQUIRED IMMUNE DEFICIENCY SYNDROME (AIDS) EXPENDITURES

	FY 1982 Actuals	FY 1983 Estimates	FY 1984 Projections, Based on President's Budget Request
NCI	$2,400,000	$3,800,000	$4,100,000
NHLBI	5,000	250,000	250,000
NINCDS	31,000	72,000	76,000
NIAID	297,000	3,150,000	4,150,000
DRR	564,000	644,000	701,000
NEI (intramural studies	33,000	45,000	58,000
NIDR (intramural studies)	25,000	25,000	30,000
TOTALS -	$3,355,000	$7,986,000	$9,365,000

Dr. **Wyngaarden**. We supported research at a total of $3.3 million in this area in 1982, estimate that we will spend approximately $8 million in 1983, and the President's 1984 budget would permit us to fund nearly $9.3 million in 1984 for research in AIDS. If one adds to that expenditures in other PHS agencies, the figure will be over $10 million for fiscal year 1983. So I think our response has been vigorous and progressive. It has involved seven or eight of our NIH institutes in various ways: The Cancer Institute in terms of Kaposi's sarcoma, the Allergy and Infectious Diseases Institute in terms of opportunistic infections, the Heart, Lung, and Blood Institute in terms of blood products, and so on. So we are broadly involved in this project and agree with you that it deserves vigorous attention.

You asked about the setasides. I would like to add that I do not believe that is necessary. I believe it could be counterproductive to sequester research funds for major medical emergencies that then would be held out from the support of research in general. Setasides tend to constrain our ability, based on increasing understanding of disease to shift resources and funds to take advantage of new information. NIH is quite capable of mobilizing the necessary funds to support work of this sort when an emergency develops.

Dr. **Brandt**. Indeed, Mr. Chairman, if I could add to that, I think that the AIDS history since 1981 when this disease was first described illustrates how the Public Health Service can in fact mount a vigorous campaign. I do not believe that there has been a single disease entity with as vigorous an attempt to try to solve the problem in the history of this country as we have put forth in this particular instance.

It involves all aspects of the Public Health Service. We have recently, as you know, issued guidelines in terms of trying to control the transmission of that disease. It is transmitted both by sexual activity and by blood and blood products. We have attempted to look at mechanisms to detect the disease, both in blood and earlier in people. We have looked at ways to treat victims and at the same time are trying to find the cause of the disease. I believe that our problem now is not that we are not putting the resources or the effort into it. It is simply that thus far nature has failed to yield up her secrets to us.

The CHAIRMAN. Dr. Wyngaarden, on behalf of Senator Eagleton, he asked me to ask you the following question. S. 773 includes language designed to insure that the programs and activity levels of the arthritis division will not be diminished by transfer to a new, separate Institute and directs the Secretary to transfer to the new Institute the personnel, assets, liabilities, contracts, property, and so on associated with arthritis, musculoskeletal, and skin diseases.

What will be the impact of this provision, both with respect to the new Institute and the remaining divisions at the Diabetes and Disgestive and Kidney Diseases Institute?

Dr. WYNGAARDEN. We can identify about $800,000 of expense, and representing 16 positions in the current NIADDK that could be transferred to a new Arthritis Institute because they are directly devoted presently to the arthritis, musculoskeletel, and skin program of the NIADDK. To transfer beyond resources that would result in a serious weakening of the NIADDK, either through a loss of 20–25 research grants or of vital administrative and management capabilities. Many of the positions that might logically be nominated for transfer involve administrative functions that are Institute-wide in character, and those individuals therefore would have to be replaced. It would seriously weaken the residual institute, including its national programs in diabetes and digestive and kidney diseases, at the expense of a new one, if more than $800,000 were to be transferred.

The CHAIRMAN. Dr. DeVita, it is a pleasure to have you before the committee again. As is the case with Dr. Brandt, you have also had the pleasure and pain of appearing before this committee on a number of occasions. My personal feeling is that some of our meetings have resulted in improvements at the National Cancer Institute.

You direct the largest and most complex of the National Institutes of Health. In fact, you direct the largest single research institute in the world. Personally, I appreciate that this is an extraordinary responsibility and requires a great deal of commitment on your part and those who work with you.

Many concerns that I have were expressed to Dr. Brandt about the committee report to S. 2311. Let me just ask one or two questions of you this morning. I am impressed with the growing evidence that diet and nutrition play a significant rôle in the cause of and perhaps even in the treatment or prevention of cancer. I am also pleased to hear that the NCI has devoted increasing efforts to research in this particular area but believe we still may be devoting too much of our research effort to palliative treatments with chemotherapy and radiation and insufficient attention to prevention. Could you please explain to us what currently is being done in the analysis of nutrition and its effect on cancer and what you believe to be the most promising areas for investigation in this area?

Dr. DeVita. Thank you, Mr. Chairman. Let me start backward and say that currently we have about $265 million that we identify as prevention research, etiology and applied prevention, and that the largest single pool of research project grant dollars go now to prevention. We are very excited about the opportunities offered by some of the findings in our epidemiology program over the last decade that diet in fact plays a major role in the etiology of cancer. As a result of these studies, we have initiated a series of prospective clinical studies to look at the effects of adding micronutrients back into the diet and some macronutrients like fiber and fat to see if in fact we can manipulate the incidence of cancer and drive it down. Some of the data that we have suggest that we might be able to see an indication of this before the end of this decade.

By 1985, as a result of a reorganization in our cancer control effort, where we now do most of our applied prevention studies, we will be funding about $18 million worth of prospective clinical studies aimed at reducing the incidence of cancer by manipulating the diet. These studies fall under the heading of chemoprevention, in the sense that we add in defined ingredients of the diet, like beta carotene, or adjust the fat content of the diet, as we are in two breast cancer studies. We are quite interested in this area, and I think it is something that could not have been done a decade ago because the data were too soft. Now the studies are there, waiting to be done, and we are very excited about getting them done.

The Chairman. I want to express the appreciation of a number of members of this committee who have been concerned about our hearings that we held in the last 2 years about the good work you have really done over there at the National Cancer Institute. I personally have been very impressed.

Dr. Brandt and Dr. Wyngaarden, I am going to try and set up a time when we can get members of the committee—it may be only myself or Senator Kennedy and I—to come out and go through completely as much as we can, in a day or so, the NIH and specifically the National Cancer Institute. As you know, in spite of those hearings we are trying to keep those funds up and trying to support you all we can. I am going to submit some more written questions to you if I can.

Dr. DeVita. Senator, let me say that while the hearings were going on and afterwards, it was always a great help to me when I was trying to urge the staff to change our organizational structure and do things a little bit differently, to always turn around and say that you were looking over our shoulders. I appreciate that.

The Chairman. We thought that might help. I want you to know, Vince, that we are still looking over your shoulders in this committee. We are starting to look over all your shoulders. It is just that there are so many of them. That is the problem. But we are going to get better at looking. The purpose is not to find fault; the purpose is to try and upgrade the situation as it exists and to try to help you, from the committee's standpoint. I know that many of you feel that you do not get an awful lot of help from congressional committees, but we hope that this one will be of some help to you. We appreciate what you have been trying to do.

Dr. **DeVita**. Thank you, sir.

[The prepared statement of Dr. DeVita follows:]

PREPARED STATEMENT OF VINCENT T. DEVITA, JR.

Mr. Chairman and Members of the Subcommittee:

I am pleased to provide this Subcommittee with information related to the reauthorization of the National Cancer Institute and to highlight the progress made possible by the National Cancer Act of 1971 and its amendments.

Those of us who are working daily to solve the cancer problem believe that the National Cancer Act of 1971 and its amendments have had great beneficial impact and must be continued. That legislation created the National Cancer Program and provided a number of important features that will continue to play vital roles in our plans for the next decade. For example:

- It authorized higher appropriations for basic research programs. Those appropriations fostered the generation of good ideas by putting more scientists to work on the cancer problem. One result is the biological revolution we now are witnessing which includes the new technologies of recombinant DNA and monoclonal antibodies.
- It established a cancer control program--a framework for technology transfer. Today this program is playing a key role in using information on cancer prevention generated in the past decade and addressing the problem of cancer prevention in a prospective way through clearly defined stages.
- It fostered the establishment of a network of cancer centers across the country. They bring the concept of the National Cancer Program--basic research and the application of the results of basic research--to each region of the country.
- It expanded our clinical trials program to study new cancer treatments. This program yielded many positive results now reflected nationwide in improved survival and decreased mortality rates for cancer patients.

- It provided training programs in research and clinical medicine that have seeded the country with cancer specialists. These scientists and physicians will assure the continued flow of research ideas and the improvement of cancer care at the community level.
- It allowed us to establish the SEER (Surveillance, Epidemiology and End Results) Program to continuously monitor cancer incidence and survival nationwide. This is critical to track our progress and to set national goals.
- It created the International Cancer Research Data Bank (ICRDB) that now serves as a valuable computerized resource for the collection and dissemination of information. The newest exciting addition--an expanded data base called PDQ--can tell community physicians who is doing the latest cancer treatments and where in their local area.
- It initiated a major effort to disseminate information to cancer patients and individuals who are at risk of cancer. The NCI and the Cancer Information Service it sponsors have responded to millions of calls and letters from the public and cancer patients.

One of the facts now apparent is that it takes at least 5 years after the infusion of resources to attract scientists, to establish laboratories and to generate ideas. Certain programs must be in place to move advances that come from the laboratories into studies that benefit people. Today, we are at the stage where the National Cancer Program is able to work at peak production.

In this statement, I describe how the programs provided by the 1971 legislation fit into a continuum that begins with basic research, moves through human studies, and ends with the dissemination of research findings to benefit people.

Prevention has been the field most affected by the National Cancer Act. We had few exploitable research leads in this area before 1971. Now we have many opportunities ready for human studies. The Cancer Control Program is the focal point for the application of the results of research in prevention. These studies have a strong scientific footing and follow a logical sequence of research steps aimed at reducing cancer incidence nationwide.

Applied prevention experiments are complicated and require four minimal components: testable hypotheses, materials to test in intervention trials, a sufficient number of trained cancer specialists (such as clinical trials and nutritional science experts, pharmacologists, epidemiologists and biostatisticians) to develop and conduct the studies, and the SEER program to monitor the results in terms of cancer incidence.

Within the next decade we should know if it is possible to prevent some forms of cancer we cannot now prevent. Cancer occurs in two stages called initiation and promotion. We now understand that most individuals exposed to cancer-causing agents (carcinogens) are not irreversibly destined to get cancer. By interfering with promotion, the later stage of causation, cancer can be prevented in animals and it appears this can also occur in humans in a suprisingly short period of time.

At least two human data sets show this is possible:

- Epidemiologists linked estrogen replacement medication with an increased incidence of uterine cancer among postmenopausal women. The FDA issued a warning and physicians followed by reducing prescriptions. Within 6 months the incidence of uterine cancer had diminished. Estrogens are a known promoter for uterine cancer.
- Data from the 1982 Surgeon General's Report on the Health consequences of Smoking show that a smoker's cancer risk approaches that of a non-

smoker's after several years of cessation. The rate at which this happens varies for different cancer sites--from 4 years for esophageal cancer, to 10 years for cancers of the head and neck, and up to 20 years for lung cancer.

One of the fruits of basic research was the discovery of antipromoters. This information came from many laboratory and epidemiologic studies. One showed, for example, that people who eat fruits and vegetables containing precursors of vitamin A, especially beta-carotene, have less cancer.

These findings have already been taken to prospective studies that will test the effectiveness of antipromoters in humans. Such studies in small, defined populations are necessary to let us to see the potential impact of a prevention strategy before it is systematically applied to the entire U.S. population.

Through our cancer control program, we started a number of prevention-oriented clinical studies in 1982 and will fund more this year. The substances we are testing--retinoids (synthetic forms of vitamin A), beta-carotene, and vitamins C and E--are readily available, inexpensive, and non-toxic when taken in the proper amount.

An additional tool that emerged from carcinogenesis research will allow us to use laboratory tests to identify persons at risk to cancer. This area of research is called "biochemical epidemiology." DNA is believed to be the point of attack for most carcinogens that initiate the cancer process. Scientists working in this field have developed tests so sensitive that they will determine whether certain carcinogens to which individuals were exposed have been taken up and actually bound to the DNA in their cells (detected at a level of one molecule of a carcinogen to each million building blocks of DNA). By incorporating this test into epidemiologic studies of populations that are potentially exposed to cancer-causing agents because of their work or lifestyles, it may be possible to identify those individuals who have been "initiated" and might benefit from exposure to antipromoters.

Another finding that may soon be ready for prevention studies revolves around the recent discovery by Dr. Robert Gallo, an NCI scientist, of the first human RNA cancer virus. He was honored by the Lasker Foundation for his work in November. The human T-cell leukemia virus (HTLV) originally came from the cancer cells of an American man with T-cell leukemia. Epidemiologic studies have now shown that this cancer, uncommon in the United States, tends to cluster in certain rural regions of Japan and in the Caribbean.

Last year, NCI scientists cloned the HTLV genome (its genetic map) in bacteria. This is the first step toward definitive studies that may provide a basis for developing another prevention strategy. For example, it may be possible to make a vaccine that could be used in the limited populations where the virus tends to cluster. This technique was responsible for the ultimate success in eradicating smallpox.

The NCI is concerned about the urgent problem of Acquired Immunodeficiency Syndrome (AIDS), which includes a rare cancer, Kaposi's sarcoma. This disease, too, appears to involve an infectious agent, although none has yet been identified. So far, the disease primarily afflicts male homosexuals in this country, intravenous drug users, Haitian entrants and hemophiliacs. Most recently, an immune deficiency which may be AIDS has been identified in children of intravenous drug abusers and in a child who received multiple blood transfusions. The incidence of AIDS is increasing at an almost geometric rate, and so far almost half of the patients have died. We have recently approved funding for new grants and supplemented others last year to study the epidemiology and treatment of AIDS. We will be issuing a request for applications for funding next year to stimulate the search for an infectious agent. This year the NCI budget for research studies on this pressing problem is $3.8 million. Next year we have planned $4.1 million.

I mentioned that the increase in appropriations provided by the 1971 Act fostered the generation of good ideas by putting good scientists to work, and that the biological revolution is one result. Scientists can now do experiments that were only dreams in 1971. It is no longer a question of whether they can map the entire complement of human genes. It is just a matter of how long it will take. The technology is at hand to compare normal genes and cancer genes. In fact, this very experiment is being done in laboratories today.

The $1 billion that supported work on cancer viruses over the past decade bought the discovery of oncogenes. The scientists who made this seminal finding also shared the prestigious Lasker award in November. Oncogenes are apparently normal genes, present in every cell of your body and mine. In fact, they appear to be present in the cells of most animals. They were captured by certain cancer viruses--pulled out of cells to become part of the viruses--which then infected other cells. In this process, the viruses altered the switch that regulates the normal genes, releasing their potential to cause cancer in experimental animals. That is how we found them. Not every normal gene has such a potential. So far, scientists have identified a limited number of oncogenes. There may be no more than 15 or 20 of them. Our best guess is that these highly conserved, important genes may be involved in the normal development process during our embryonic growth and shut down normally in adult life only to be activated by a cancer-causing event.

Most recently, an extraordinary observation has been made by geneticists. They found oncogenes to be associated with rearrangements of chromosomes--

structures in the nucleus of cells that carry genes--that occur consistently in the cancer cells of many cancer patients, among them patients with Burkitt's lymphoma and chronic myelocytic leukemia. This finding reinforces the hypothesis that oncogenes--located in the wrong place by accident or switched on in an unusual way--play a role in cancer causation.

Even now scientists are synthesizing the products of these oncogenes. We will soon know if they can become a new target for diagnosis, prevention, and treatment of cancer. This would be a paradigm change of the first order and may make all our present methods obsolete.

This dizzying pace of science during the past decade has brought molecular biology to the bedside. This even closer approximation of basic and clinical science will be the hallmark for the 1980's. If we are to exploit oncogenes, monoclonal antibodies, and cancer prevention studies, molecular biologists will have to work closely with clinicians.

This is not necessarily a natural liaison. In an attempt to foster such relationships in cancer treatment, NCI will establish national drug discovery groups. These think tanks of industry and academic scientists will assure that cancer drug development keeps pace with the new molecular targets identified by modern molecular biology. Instead of relying solely on the directed, but somewhat random process we have been using to identify new drugs, the drug discovery groups will suggest new, more specific targets identified at the molecular level.

In fact, we already have identified new targets. Pharmacologists have found that cancer cells have a certain intuitive behavior that allows them to bypass the killing effects of our best cancer drugs without ever being exposed to the drug. This is the major cause of treatment failure with drugs. Knowing the path offers us new opportunities to exploit it. Such studies are already in progress in the clinic.

Those treatment advances now benefiting people are the result of the many clinical trials NCI has supported through cooperative groups and cancer centers. These have been molded and modified since 1974. I mentioned the cadre of medical and radiation oncologists that emerged from the training programs provided by the 1971 Act. They are now practicing in every community in the United States. And this has given us a unique opportunity to integrate clinical trials with the practice of cancer medicine and to diffuse advances in treatment as they are being developed.

This year we will fund about 100 Community Clinical Oncology Programs, or CCOPs. They are designed to reach the 80 percent of cancer patients who are first seen by physicians not trained in oncology and treated in their home communities. The CCOPs, with the help of the PDQ computerized information system, will integrate the many specially trained community physicians with cancer centers and the large cooperative groups that conduct treatment studies.

The PDQ data base provides information in a user-interactive format. It draws on computerized lists of experts and clinical investigators to tell physicians who is doing what and where within a geographic matrix. This final link in the National Cancer Program clinical treatment effort offers the promise of rapidly decreasing national mortality with existing treatment by closing the gap between what we can do and what we actually do.

It is a pleasure to report that progress has been made and is everywhere evident. This year our SEER program reports that fully 46 percent of patients with the serious cancers survive their disease 5 years and many of them are cured. The national cancer mortality rate decreased during the 1970's for Americans under the age of 45. For some sites, the decrease is the result of improved treatments:

- For ovarian cancer, the national mortality rate fell 38 percent because of better staging of patients and wiser application of existing chemotherapy and radiotherapy;
- For premenopausal women with breast cancer, a 15 percent decline is attributable to the application of adjuvant chemotherapy;
- For testicular cancer, a 43 percent decline is the result of new drug therapy introduced in 1976. That advance, along with the radiation used as standard treatment for one form of the disease, makes testicular cancer curable in most cases--even when diagnosed in the most advanced stages;
- For Hodgkin's disease, a 56 percent decline in the mortality rate, and for other lymphomas, a 29 percent decline, are due to combination chemotherapy; and
- For bone cancer, a 19 percent decline is because of overall better application of surgery, radiation therapy and cancer chemotherapy in these patients.

These decreases in mortality related to treatment advances took a minimum of 5 and most often 10 years to occur on a nationwide basis because of slow diffusion of new information to physicians not trained in cancer management. It is this gap we hope to reduce to one year this summer with the completion of the PDQ system.

- For lung cancer among men, the decrease in mortality is due to prevention and shows cancer can indeed be prevented. An 18 percent decline is attributable to the success of smoking cessation campaigns.
- For cervical cancer, early detection is responsible for a decreased incidence of invasive disease and decreased national mortality. The mortality rate for cervical cancer has fallen by 47 percent.

Mr. Chairman, this is an age of opportunity in cancer research. We are at this stage today because of the National Cancer Act of 1971 and its amendments. The resources, instruments, and flexibility provided by that legislation--the great support for basic research, the cancer centers, the cancer control program, the training programs, the SEER registries, the ICRDB and, most recently, PDQ--are providing the tools needed to translate the findings of basic research into widespread applications.

We feel the Act and its amendments have served us well over the past decade. They gave the NCI Director the flexibility and authority he needed to carry out the Act's special provisions, while maintaining excellent and productive working relationships with the NIH. The maintenance of these authorities in their present form is essential for continuing the momentum of the National Cancer Program.

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The CHAIRMAN. Dr. Lenfant, it is a pleasure for me to welcome you here today as well. It is the first time that you have appeared before the committee, as director of the National Heart, Lung, and Blood Institute. This is the second largest institute at NIH, and you have the responsibility for an enormous array of research, covering a broad spectrum of medical diseases.

I understand from your previous work at NHLBI that you are well aware of the challenges and opportunities facing you, and I also understand and feel very good about your exceptional qualifications to serve as the director. So we are very pleased to have you there.

Could you briefly cite for us the most promising areas of research in NHLBI with respect to what remains our number one killer, heart disease?

Dr. LENFANT. Thank you for your kind remarks, Mr. Chairman. Cardiovascular diseases, as you know, are a very important public health problem in the United States. Before I answer your question, I would like to share with you what I consider to be a very important piece of good news.

We know that for the first time since 1949, cardiovascular diseases have dropped to less than half of all the deaths in the United States. Further, we also note today that, in the age group of 35 to 45 years of age, there has been a decline of about one-third in the death rate due to cardiovascular disease. This, to us, reflects the vitality of our program.

To answer your question, I would like to point out that there is no single approach which is more important or successful but rather an array of approaches. Our institute is very actively engaged in the acquisition of new knowledge. Today, we have new opportunities in molecular biology and cell physiology that we are capitalizing on. Genetics now has become a tool that we are exploiting. Further, another approach that we are using and pursuing very actively is the testing and evaluation of new interventions and new knowledge. As you know, Mr. Chairman, our institute has been very keen on fostering clinical trials and experimenting with new technology.

At this point, it is especially timely to mention our work in the areas of the artificial heart and other circulatory assist devices that our institute supports. I might even show you one such artificial heart that I have brought with me.

The CHAIRMAN. We love the support that you are giving to the University of Utah. We want to see that it continues. In fact, all of you can do much more than you have done in the past.

Dr. LENFANT. We are working on it, and I can assure you that the University of Utah, too, is working at it.

The third approach that I would like to mention, because we think it has been extraordinarily successful, especially with regard to high blood pressure, is our dissemination of existing and new knowledge.

In summary, Mr. Chairman, I find it difficult to identify just one direction which is important to our programs. I would like to say that we think that the multiplicity of our approaches is what has led to the success reflected in the decline in mortality rates that I mentioned earlier.

[The prepared statement of Dr. Lenfant follows:]

PREPARED STATEMENT OF CLAUDE LENFANT

As the new Director of the National Heart, Lung, and Blood Institute (NHLBI), I am pleased to provide this statement for the record. In the eleven years since the enactment of the National Heart, Lung, and Blood Act, P.L. 92-423, the NHLBI has achieved important advances in prevention, diagnosis, and treatment of diseases which are major causes of death and disability in this country. In fact, of the diseases that are of concern to this Institute, four are among the ten leading causes of death in the United States today: heart disease (first), cerebrovascular diseases (third), chronic obstructive pulmonary diseases (fifth), and atherosclerosis (ninth).

Health and Economic Impact: Together, the cardiovascular and lung diseases account for over 1 million deaths annually. Approximately 40 million Americans have diseases of the heart and blood vessels. Cardiovascular diseases remain the leading causes of death in the United States for men beginning at age 40 and for women beginning at age 60. These diseases account for 30 percent of all the potential years of life lost to illness. Furthermore, heart disease alone accounts for more bed days than any other condition. The total economic burden of cardiovascular disorders is estimated to be over $80 billion in 1979. This is more than one-fifth of the total cost of illness in the United States. The social and economic toll of diseases of the lungs and respiratory system is equally severe and rising rapidly. They account for more than 5 percent of all the potential years of life lost as a result of illness. The total economic costs for lung and related respiratory diseases was over $21 billion in 1979, six percent of the total cost of illness. However, these diseases are the leading cause of morbidity costs, representing almost 18 percent of the total.

Blood diseases frequently strike during childhood and standard economic measures cannot fully reflect the costs in terms of suffering and grief. These diseases, including the hemoglobinopathies, cause or are manifested in a variety of serious disorders and their true impact is far greater than can be expressed in terms of mortality. In those afflicted with serious chronic blood diseases, death is often attributed to acute superimposed conditions. In addition to the importance of blood diseases, the blood and blood components play an essential role in general medical and surgical treatment, with 10,000,000 units of blood and packed cells used in the treatment of more than 2,700,000 Americans annually.

Despite this dire picture, it is encouraging to note that in 1982, for the first time since 1949, cardiovascular disease has dropped to less than 50 percent of all deaths in the United States and that in the age group 35 to 45 there has been a 36 percent decline in deaths within the last decade. Recent advances in heart, lung and blood research give us reason to anticipate that within the next decade we will be able to speak less of deaths from these diseases and instead will be able to emphasize health gains in more positive terms, such as the number of people with disease who have an improved quality of life, or the number of diseases we are able to prevent.

Stategy to Achieve the NHLBI Mission: The program strategy employed for each of the disease-related mandates of the NHLBI consists of an ordered sequence: (1) acquisition of new knowledge, (2) testing, evaluation and validation of promising hypotheses and methods of treatment and prevention, and (3) dissemination of new and existing knowledge. The past eleven years have seen major breakthroughs in the diagnosis, treatment and prevention of heart, lung, and blood diseases, advances which are the result of discoveries made in a large number of studies of various kinds. Although newsworthy surgical and pharmacologic interventions have frequently provided evidence of recent accomplishments, it has been the strong, consistent, balanced program of laboratory and clinical studies supported by multiple mechanisms, i.e., investigator initiated research grants, clinical trials, and contracts, that have provided the essential resources for each major advance.

As the foundation of the Institute's program, basic research on disease etiology and pathogenesis received the major portion of Institute resources. This research has resulted in a number of significant concepts, theories, and discoveries which, in turn, have become the foundation for further research. I would like to briefly mention some examples of progress in cardiovascular, pulmonary, and blood disease research.

Cardiovascular Disease: Coronary heart disease and its precursor, atherosclerosis, are the major contributors to the death and disability of Americans. The ultimate goal of our national research program in atherosclerosis is prevention of the process itself and of the associated sickness, disability, and premature death. To achieve this long-range goal, a large research effort operates on several fronts simultaneously: clarification of the nature and pathogenesis of the process, elucidation of predisposing and causative factors, and intervention to safeguard individuals and populations.

Research in cell and molecular biology has provided much new and exciting information about the cells of the arterial wall. For example, it has been possible to induce changes in cultured vascular cells similar to those observed in experimentally induced atherosclerotic lesions in intact animals, such as nonhuman primates. Fresh approaches, such as cell culture, have made it possible to examine interactions between blood components (for example, lipoproteins, platelets, or hormones) and the individual cells of the arterial wall, and to assess conditions that promote, or reverse, atherogenesis. The use of cultured vascular cells has also made it possible to identify inherited cellular abnormalities that lead to atherosclerosis, to define cellular metabolic pathways for lipids, and to discover factors that regulate the growth of arterial cells. Since atherosclerosis results from cholesterol accumulation in arterial walls, understanding how its levels are regulated has important implications for the prevention of coronary heart disease. The major vehicle for transporting cholesterol in blood is the low density lipoprotein (LDL). They are processed by specific LDL receptors on cell surfaces that not only remove them from blood but release the cholesterol that then becomes available for normal metabolic functions within the cell. The production of LDL receptors is regulated by the cholesterol content of the cell, the number of receptors increasing as cholesterol content decreases. It is, therefore, of great interest that a genetic defect in familial hypercholesterolemia leads to an absence of normal numbers of LDL receptors. This observation suggested the possibility that using a new drug, an Acetyl CoA reductase inhibitor, that specifically inhibits cholesterol synthesis, might correct the abnormality in number of LDL receptors in familial hypercholesterolemia. Animal and early clinical studies of this drug have been successful enough to indicate that it might become a powerful tool for treating familial hypercholesterolemia and provide a better understanding of the role of metobolic processes in health and disease.

Pulmonary Diseases: The pulmonary diseases within the purview of the Institute fall into two broad categories: those in which loss of respiratory function is a consequence of destruction of lung tissue, and those in which the loss results from proliferation of tissue. As recently as a decade ago we knew there was impaired function and were able to quantify its severity, but we did not know the etiology and pathogenesis or how to arrest the progressive degeneration. Today we can point to major insights into the events that initiate the disease process and into many of the steps involved in its progression.

Interstitial lung fibrosis is characterized by thickening of alveolar walls due to excessive or 'irregular' deposition of collagen fibers which eventually replace the alveolar spaces and contribute to restrictive lung dysfunction. Emphysema, also a debilitating lung disease, is manifested where dilation of air spaces of the lung results from destruction of alveolar walls. This is a consequence of degradation of the supporting connective tissue and leads to a progressive deterioration of lung function and marked airflow obstruction. Thus, although fibrosis and emphysema appear to be separate clinical entities, each with distinct biochemical, radiological, and pathological characteristics, they share a common pathogenic feature; namely, modification of connective tissue proteins following the primary injury. Recent studies indicate that it is possible to direct the pathogenic events experimentally to progress either to pulmonary fibrosis or emphysema in the same set of animals by appropriate manipulations. In these studies, intratracheal administration of cadmium chloride to hamsters caused an acute lung injury which subsequently evolved into diffuse fibrosis. However, with the simultaneous feeding of B-aminoproprionitrile, which is a metabolic poison that interferes with normal collagen and elastin synthesis, the injury might lead to either a proliferative or destructive disease, depending upon the superimposition of secondary insults. This finding has potential value toward elucidating the pathogenesis of fibrosis and emphysema, as well as toward developing rational approaches to their therapy.

Clinical studies have shown that calcium channel blockers (a group of new drugs which block the flow of calcium into cells and interfere with the calcium-dependent contractile mechanisms in a variety of tissues) are useful in the control of coronary artery spasm. They have also been reported to prevent exercise-induced bronchoconstriction in asthmatic subjects. Recent animal studies have provided evidence that bronchospasm induced by histamine, one of the most potent allergic mediators, can be blocked by a calcium channel blocking drug. It appears to block bronchoconstriction in both large and small airways; however, the resting muscle tone in the airway does not seem to be altered. Although it is postulated that the drug acts directly on bronchial smooth muscle and that it may also inhibit the release of allergic mediators from mast cells, the exact mechanisms by which the drug interferes with the activation of bronchial smooth muscle are not yet understood. Drugs that can act as bronchodilators without stimulating cardiac muscle, and conversely, those that relieve angina without producing bronchoconstriction are needed in clinical practice. Such agents would be invaluable in treating the large number of patients who have both chronic airway obstruction and coronary artery disease.

Blood: Inherited structural differences in the hemoglobin molecule are widespread and numerous. Two such inherited conditions, sickle cell anemia and Cooley's anemia, are common manifestations associated with profound disability and premature death. The consequences of fundamental research on hemoglobin, however, reach far beyond improved management and therapy for these hemoglobinopathies. Insight and understanding of human genetic disease in general, of the pathophysiology of oxygen transport, of the nature of protein synthesis, even of the mechanisms of red cell destruction, all derive in some measure from basic research on hemoglobin.

A recent investigation illustrates how studies of molecular biology and gene expression have resulted not only in new knowledge but in a clinical application. A drug used to modify the expression of a gene has the potential of correcting a hemoglobin abnormality that characterizes sickle cell anemia and thalassemia (Cooley's anemia). Preliminary results indicate that this drug corrected some of the physiologic abnormalities in thalassemia patients. In both of these blood disorders hemoglobin in the fetus is normal, but the hemoglobin that enters the bloodstream after birth lacks specific subunits essential for normal function. In a study designed to replace the abnormal globin subunits with those found in fetal hemoglobin, investigators used 5 Azacytadine (a drug used in cancer therapy) to "turn on" the genes for production of fetal hemoglobin. In animal studies, and subsequently in a few patients, the hemoglobin had subunits typical of normal fetal hemoglobin and patients experienced considerable physiologic improvement. This very promising development is being pursued to determine whether such a regimen is effective and safe enough for wider clinical use.

Prevention: We regard the biomedical spectrum as one embracing knowledge acquisition, knowledge validation, and knowledge transfer. Until the findings of our basic and applied research are utilized in such a way as to prevent, reduce, or ameliorate the disease with which we are concerned, we have not completely responded to the mandate and our mission. That is why we give considerable attention to such issues as the effective transfer of our research findings in order to appropriately influence relevant decision-making by both the health professions and the public. Let me share a few examples which will illustrate the range of our activities in this area.

It is now a little more than a decade since the Institute was legislatively mandated to implement prevention, education and control programs. It has also been the same length of time since the Institute was directed to develop and operate a national program to control high blood pressure in the United States.

The high blood pressure effort--which evolved into the National High Blood Pressure Education Program--represents the Institute's major prevention-related activity. Since its inception, there have been many positive changes in the detection, treatment and control of high blood pressure. During the past 10 years, we have seen a much better understanding of high blood pressure fostered among the public; the development of a better educated health profession able to provide more effective treatment of high blood pressure; and, the evolution of a much improved therapy regimen largely resulting from pharmacological research. Numerous opinion or awareness surveys, trends evidenced by changes in prescribing practices of physicians, increased patient visits for hypertension, etc. all testify to the progress of better high blood pressure control in this country. Perhaps, the most dramatic indicator is that of stroke mortality. Since the program began, stroke mortality has been dropping by about five percent per year. That represents thousands and thousands of lives that would have been lost to stroke, had not the decline taken place. While it may be an overstatement to say there is a cause and effect relationship between the program and the mortality decline, high blood pressure is clearly the primary cause of stroke in this country.

This year, we will be observing the tenth year in the National High Blood Pressure Education Program. Fittingly, the National Conference on High Blood Pressure will be held in Washington this April with the theme--"A Decade of Progress - The Challenge Ahead."

While the national high blood pressure effort has been our major disease intervention effort, it has not been our only activity in this area by any means. I would like to highlight a few recent projects in the disease prevention and health promotion area.

In the area of smoking cessation, we have developed a quit-smoking demonstration program which attempts to utilize the reach and the power of television and merge it with the more personalized resources of community programs. Ideally, the program would have local sponsorship. The "on air" TV staff, preferably newscasters, would attempt to quit smoking and urge viewers to follow suit. Each night, the quit-smoking segment would attempt to provide the viewer with encouragement and skills to help stop the smoking habit. The Institute, in conjunction with the American Lung Association, has successfully tested the approach in Minnesota and is currently evaluating its benefit in a number of locations. Another prevention-related program ready for broader dissemination is that of the self-management of asthmatics. The Institute supported three studies which attempted to demonstrate the value of instructing asthmatic children, their parents, teachers and others close to the children, in detecting early warning signs of impending asthmatic attacks and educating them as to what precise steps to take to avert the attack. In all three studies, it was demonstrated that a vigorous instructional program can lead to fewer asthmatic attacks as well as to a lesser demand on medical services. We are currently developing plans to take the essential lessons of these three demonstration programs and effectively transfer them to health care professionals and others who can apply them at the local level.

How to effectively transfer the lessons of positive demonstration programs into settings where there will be a broader application is an ongoing challenge to the Institute. A few years ago, we initiated demonstration projects at Ford Motor Company, Westinghouse and the State of Maryland to ascertain whether the worksite was an effective setting in which to bring hypertensive employees under control. These projects were completed within the past year and the results make a strong case for the value of worksite programs. The ability to keep hypertension under control was seen as about three times greater at the worksite than in the community. Conveying this information and similar data to those in the corporate structure who could decide whether or not to initiate worksite programs was a job that we felt we could not do alone. General Motors and Metropolitan Life have agreed to join the NHLBI in sponsoring a conference, to be held later this year, which will be designed to make the chief executive officer of selected companies aware of existing data which make a strong case for investing in employee health programs.

In summary, over the past eleven years NHLBI has made great strides towards understanding the etiology and pathogenesis of cardiovascular, pulmonary and blood diseases. With the advice and support of this committee and our focus on a balanced program of knowledge acquisition, validation and transfer the prevention of these diseases is a hopeful prospect for the future.

The CHAIRMAN. We are very appreciative of that. I am going to submit some questions to you in writing as well. We appreciate your being with us here today.

Dr. Salans, it is also a pleasure to have you before the committee again. As Director of the National Institute of Arthritis, Diabetes, Digestive, and Kidney Diseases, you have the considerable achievement of representing the only institute that some of us here in Congress want to shakeup. I hear from many sources that you are really doing an elcellent job.

My interest in proposing the new arthritis institute certainly has nothing to do with your management. I have recently met with directors of the Advisory Board for Diabetes, Arthritis, and Digestive Diseases. They all cited concerns about inadequate funding for their research effort. Could you tell the committee how the budget for these areas of research is allocated?

Dr. SALANS. Yes, Senator Hatch. I am very pleased to have the opportunity to discuss that. Of course, in allocating dollars in the institute, the first thing that we pay attention are the congressional mandates and directives and the intent of Congress. As you know, there often can be direct mandates to the institute to allocate appropriated funds to a certain area of research. We respond to those directives and to congressional intent.

Of course, each year we also have to meet our obligations that have been incurred in each of our program areas from the previous years. Once those two things have been done, we then have a few dollars left to allocate among our various disease programs. I would say that the primary driving force in how those dollars are allocated is the research activity and the scientific merit of the research in each of these fields. An area that has a highly active research program where applications of good scientific merit are coming into the study sections and then to the institute will receive a greater allocation of funds than will areas of less meritorious science and less demand. So, scientific merit is the primary driving force.

I would note that this approach can be modified and that we do take into account special needs and special opportunities in each of our program areas. We work with our National Advisory Council and other advisors to identify when a special or particular opportunity or need arises, so that we can modify our allocation process. We have, over the last year or year-and-a-half, since the institute has become a bureau, developed a new allocation process which allows us to monitor throughout the year how funds are being used and whether or not in fact we are able to take advantage of the opportunities and the demands that are being placed upon our budget. Through this process, we reallocate funds if in fact imbalances do occur. I am happy to say, Mr. Chairman, that this process is working extremely well. Over the last year or two, we have had good program balance, good balance in the scientific merit and numbers of grants that have been funded in each of our program areas.

Finally, let me say that, as long as we have been talking about arthritis this morning, the new process of allocating of funds has been of particular direct benefit to the arthritis research community. In 1982, a year in which the Institute's budget was reduced by

$1 million, the only research activity area that did not share in the reduction was the arthritis division. That was the result of applying the new allocation process that I have described to you.

I think we have a fair and equitable way of distributing the dollars among the programs, one that allows us to fund the best science and the best scientists and to maintain appropriate balance among our various disease areas.

[The prepared statement of Dr. Salans follows:]

PREPARED STATEMENT OF LESTER B. SALANS

Mr. Chairmen and Members of the Committee:

I am very pleased to have the opportunity of submitting this statement for the record and of describing the research activities and accomplishments of the National Institute of Arthritis, Diabetes, and Digestive and Kidney Diseases (NIADDK). I will focus first on the extensive mission of NIADDK and provide some examples of the Institute's many research accomplishments. Because of the Committee's particular interest in the arthritis-related programs of the Institute, I will also describe how the NIADDK organization, as well as recent managerial initiatives, are enhancing arthritis research efforts.

Scope of Research Responsibility

The National Institute of Arthritis, Diabetes, and Digestive and Kidney Diseases (NIADDK) supports and conducts research on some of the most serious diseases affecting the health of our nation's citizens. The diseases for which the Institute bears research responsibility are among the most common, debilitating, and costly in the United States. Over 31 million Americans suffer from different forms of arthritis. Approximately 11 million adults and children have diabetes and approximately 300,000 die annually from the disease and its complications. Chronic digestive disorders affect twenty million Americans. Digestive diseases cause about 200,000 deaths annually and hospitalize more people than any other group of diseases. Kidney disease claims the lives of over 50,000 Americans each year. In 1982, over 70,000 end stage renal disease patients were kept alive by dialysis or transplantation under the Medicare program at a cost of about $1.8 billion. The collective economic burden of the diseases addressed by this Institute exceeds $70 billion annually.

To conquer these diseases, the Institute sustains a far-ranging, multidisciplinary research program characterized by excellence, innovation, and productivity. A strong foundation of basic research is complemented by vigorous clinical research on the diseases of internal medicine and dermatology and surgical disorders of the skeletal and urological systems.

Strong interrelationships exist among different Institute programs, which depend on common scientific threads like metabolism, endocrinology, immunology, and molecular genetics. Enormous advances in these areas are now being successfully applied to the study of all the diseases within the Institute's research mission.

Highlights of Research Progress

Investigator-initiated research grants are the cornerstone of the Institute's activities, representing over 60 percent of NIADDK research efforts. At the same time, NIADDK gives special emphasis to research training and manpower development, recognizing the need to continuously replenish our nation's research talent.

Through vigorous support of research and research training, the Institute is making major contributions toward improving the nation's health. I would like to cite at least one example of research progress in each of the Institute's categorical disease divisions.

In the Division of Arthritis, Musculoskeletal and Skin Diseases, researchers have discovered abnormalities in the immunological system of patients with rheumatoid arthritis and systemic lupus erythematosus (SLE), providing opportunities for the future development of new therapies to correct specific defects of the immune system in the treatment of these arthritic disorders.

In the Division of Diabetes, Endocrinology and Metabolic Diseases, researchers are identifying genetic and immunologic defects that may indicate that an individual is susceptible to, at high risk for developing, or in the earliest stages of the two major types of diabetes mellitus. If these or other specific abnormalities can be confirmed to play a causative role in diabetes, it may be possible to modify the expression of the abnormal genes or immunopathology and prevent certain types of diabetes.

In the Division of Digestive Diseases and Nutrition, researchers have shown that some patients with long-term chronic active hepatitis have incorporated in the genetic apparatus of their liver cells the DNA of the virus that causes hepatitis B. The same viral DNA was found in some patients with liver cancer, who previously were hepatitis B carriers. These findings suggest that the recent development of an effective vaccine against hepatitis B may thus contribute to marked reductions in liver cancer.

In the Division of Kidney, Urologic and Hematologic Diseases, research has led to the development of a comprehensive approach to the evaluation and treatment of kidney stones, a major achievement in research related to the urinary tract. Tailor-made medical therapies now can be used to prevent the recurrence of up to 80 percent of various types of kidney stones in patients who are habitual stone-formers. End stage renal disease is also a primary focus of the Institute's kidney research efforts and the basis of two major scientific initiatives. Through our first initiative, we will support new research projects to explore the natural history and mechanisms of the chronic kidney diseases that frequently lead to ESRD, in an effort to prevent kidney failure. Our second initiative will attempt to identify objective criteria for initiating maintenance dialysis in ESRD. This research may enable physicians to determine more precisely in each patient when dialysis should be initiated, and to tailor dialysis better to individual needs.

Contributing to the success of these research efforts are the many special activities and programs which the Congress has established for NIADDK disease areas. These authorities are supported by the NIADDK community and the Institute supports their reauthorization.

Through multipurpose centers, the Institute has been able to stimulate collaborative research, education, and community programs in arthritis and diabetes at leading research institutions throughout the United States. The Institute's research programs in arthritis, diabetes and digestive diseases have been guided by national commissions established by Congress to develop long-range plans for each of these diseases and, more recently, national advisory boards have continued to assess and make recommendations regarding efforts to combat arthritis, diabetes and digestive diseases. Complementing the activities of the boards is the work of three interagency coordinating committees designed to coordinate all NIH research on arthritis, diabetes and digestive diseases; to assure the adequacy and technical soundness of all Federal activities in these areas; and to provide for the full communication and exchange of information necessary to maintain effective coordination of such programs.

At the same time, the Institute's research efforts are also benefitting from a variety of administrative actions. Perhaps most important of these is the recent elevation of the Institute to the status of a bureau within the National Institutes of Health and the creation of six major operating divisions within NIADDK. Through bureau status, each of the Divisions of NIADDK is achieving greater visibility, prominence and autonomy. Each Division now has the capacity to establish and strengthen a Division Advisory Council as part of the Institute's National Advisory Council. In addition, elevation to a bureau has enhanced the stature of NIADDK as a whole, both within NIH and the Department, and has substantially increased NIADDK management capabilities.

In this regard, several new management initiatives have been undertaken by NIADDK since my appointment as Director which provide for greater visibility and strength of each of our program Divisions and an enhanced capacity of the Institute to interact with and be responsible to the needs of the external community. Prominent among these has been the establishment of the Institute as a Bureau with four extramural program Divisions: the Division of Arthritis, Musculoskeletal and Skin Diseases, the Division of Diabetes, Endocrinology and Metabolic Diseases, the Division of Digestive Diseases and Nutrition, and the Division of Kidney, Urologic and Hematologic Diseases.

A major change has been made in the NIADDK budget allocation process which represents, in our view, a significant managerial improvement. Budgeting is now done by Division, permitting the Institute for the first time to achieve balanced support of its Divisions and Programs. The new process permits the Institute to make adjustments throughout the year, which provide the necessary flexibility to take advantage of special needs and opportunities that present themselves throughout the year.

This new budget process and other managerial initiatives reflect both the willingness and the ability of the Institute to respond administratively to scientific needs and opportunities, as well as public and Congressional concerns.

Research on Arthritis, Musculoskeletal and Skin Diseases

Recognizing the Committee's interest in arthritis-related research, I would like to describe in detail the Institute's strong and continuing commitment to research in this area.

Arthritis research is a cornerstone of this Institute and an area of intense scientific activity and progress. It is now clear that arthritis is not a single disease, but rather a group of perhaps 100 or more disorders with many different causes, including genetic, immunologic, inflammatory, and infectious factors. We are gaining a better understanding of the vital role of the body's immune defense system in rheumatoid arthritis and other rheumatic diseases. In patients with rheumatoid arthritis, a specific defect has been found in cells of immunologic system that normally suppress the body's ability to produce antibodies against the virus associated with infectious mononucleosis. This finding provides an important new insight into the immunologic basis of rheumatoid arthritis and may lead to development of specific immunologic treatments. New knowledge about the role of various mediators of inflammation is also increasing our understanding of the inflammatory processes involved in rheumatoid arthritis. Research on the cause of osteoarthritis includes promising biochemical and metabolic investigations. Recently, new knowledge has been gained concerning development of the earliest lesions seen in osteoarthritis.

NIADDK Budget for Arthritis, Musculoskeletal and Skin Diseases

Since 1976, funds expended by the Arthritis, Musculoskeletal and Skin Diseases Division have more than doubled. Using 1976 as a base year (1976=100%), the Arthritis Division is growing more rapidly on a percentage basis than any other Division in NIADDK and greater than NIH as a whole.

As a consequence of the Institute's new budget process, in FY 82, when the Institute sustained a net loss of $1 million, funds for the Division of Arthritis, Musculoskeletal and Skin Diseases were kept stable, while other programs absorbed the reduction.

Only a tentative budget allocation has been developed for FY 83. As in FY 82, the allocation will be modified throughout the year according to scientific needs and opportunities presented. This will allow the Institute to respond to special opportunities in arthritis research. The new budget process will also provide the Arthritis Division with greater flexibility in allocating its dollars among its respective programs, and in increasing its responsiveness to emerging scientific leads. Under the tentative FY 83 budget, funds for the Arthritis Division will increase about $8.6 million from the FY 82 level of $72 million.

Clearly, there are many serious diseases for which interest groups are seeking to obtain greater visibility and resources. Competition for funds is keen, and there is a need to maintain an appropriate balance among the many programs of the National Institutes of Health.

New Initiatives in NIADDK Arthritis and Musculoskeletal Diseases Programs

Following are examples of new initiatives in arthritis and musculoskeletal diseases, which the Institute plans to undertake:

- o Announcement soliciting applications on the etiology of rheumatoid arthritis;
- o Announcement soliciting applications in a musculoskeletal diseases research area identified through the Institute's current detailed evaluation of this field, which will be completed in 1983;
- o Development of two specifically targeted new training awards in arthritis and musculoskeletal diseases: the Special Emphasis Research Career Award and the Physician Investigator Development Award;
- o Development of a trans-NIH arthritis program with lead responsibility in the Director of the Division of Arthritis, Musculoskeletal and Skin Diseases, NIADDK. This program will identify, encourage, and highlight arthritis and musculoskeletal diseases-related research in other NIH institutes.

Relationship of Arthritis to Other NIADDK Programs

Within the current NIADDK organization, close, strong and productive interrelationships exist among all categorical disease programs, with common threads of basic research underlying all of the Institute's disease areas. All of our disease areas benefit from close and procuctive collaboration, and this is particularly so for arthritis research.

One of the many forms of arthritis that primarily affects women is systemic lupus erythematosus (SLE). This disease affects many organs of the body. Lupus nephritis affects the kidney and is of special concern to the NIADDK kidney program. Lupus also affects the skin and hair and is under study by the skin diseases program. The treatment of lupus with adrenal steroids is closely related to basic research on these compounds in the endocrinology and metabolic diseases programs of the Institute. Blood-cell abnormalities in lupus are under investigation by scientists in the hematology and nutrition programs.

Like rheumatoid arthritis, the underlying causes of SLE appear to be genetic and immunologic. Genetic and immunologic abnormalities similarly lead to diabetes mellitus, certain forms of kidney diseases that result in kidney failure, various diseases of the endocrine glands, inborn errors of metabolism such as cystic fibrosis, and diseases of the digestive system and liver. Research supported by NIADDK in each of these categorical disease areas is following similar tracks with regard to presumed causative genetic and immunologic factors. Like arthritis, diabetes is a disease that disproportionately afflicts the aging population. Research into the factors responsible for this common characteristic is closely interrelated in this Institute. These kinds of collaborative efforts benefit from the research climate that now prevails in the Institute as currently organized, and would not be as productive in a more narrowly defined and separate institute.

Trans-NIH Arthritis Research Efforts

Cooperative ventures in arthritis research are also occurring among NIADDK and other NIH institutes:

A new disease, Lyme arthritis, was discovered in the mid-1970's and traced to an infectious organism (spirochete) carried by a tick. It is being examined as a model for the study of infection as an initiator of arthritis by scientists in both NIADDK and in the National Institute of Allergy and Infectious Diseases.

Similar collaborative opportunities exist between other institutes. For example, NIADDK and the National Institute on Aging share an interest in osteoarthritis and osteoporosis. Juvenile arthritis can be addressed by NIADDK and the National Institute of Child Health and Human Development. The immunologic basis of rheumatoid arthritis and SLE is of concern to both the NIADDK and the National Institute of Allergy and Infectious Diseases. NIADDK is making vigorous efforts to enhance cooperative initiatives in arthritis research among relevant NIH institutes and to promote a trans-NIH arthritis program.

Conclusion

The programs of the NIADDK are strong, innovative, and highly productive. With new leadership, and continued public and congressional support, the Institute is making substantial progress to address its extensive research mission in the most efficient and effective manner possible. We view the 1980s as a period of vast scientific opportunity and accelerating research momentum. We plan to take full advantage of the many emerging scientific leads in arthritis, diabetes, digestive diseases, kidney disease and other institute programs, so that the benefits of NIADDK research can be effectively applied to improve the health of our citizens.

The CHAIRMAN. That is terrific. I will submit some questions to you as well, Dr. Salans.

Dr. Cummings, we are happy to have you here also. In the committee report accompanying S. 2311, we were concerned about the library not keeping abreast with new technology and information transfer. As you know, there has been a virtual revolution in this area over the past few years, and I would like to know what steps have been taken to facilitate a more efficient and potentially economic transfer of current medical information to our libraries and physicians throughout the country. If you could just give us a few remarks on that, I would appreciate it.

Dr. CUMMINGS. Yes, I would be very pleased to respond to that question, Senator Hatch. We have for the past decade provided both financial and technical support to our Nation's medical libraries, creating a library network which joins the resources of the larger institutions with those of the smaller institutions so that resources can be shared through new computer and communications technologies. In fact, the National Library of Medicine has developed an integrated library system which can operate on many small computers, which makes it possible for small community hospitals as well as academic health centers libraries to use modern computer technology in managing the vast array of informational materials that are flooding health and medicine.

I believe that the advantages that are provided by our society in creating new technologies are being rapidly applied for better medical information and dissemination. One of the deficits in our program is the dearth of physicians and other health professionals who are trained in the field of medical informatics. That is to say, I think our Nation, amongst others, is deficient in having sufficient people trained to apply these new technologies on behalf of public health, patient care, medical research, and health education.

[The prepared statement of Dr. Cummings follows:]

PREPARED STATEMENT OF MARTIN M. CUMMINGS

Medical Library Assistance Act
Statement for the Record

I am pleased to have this opportunity to provide for the record a statement in support of reauthorization for the Medical Library Assistance Act.

The benefits from the national investment in biomedical research can be realized only to the extent that the new information and knowledge is transferred to biomedical scientists, medical educators and health care practitioners at appropriate sites and in effective formats designed to enhance its utilization in the delivery of health care.

In an attempt to facilitate the dissemination and use of research findings to health professionals, the Medical Library Assistance Act (MLAA) was authorized by Congress in 1965. Numerous studies had shown that the Nation's health-science libraries were in a state of disarray: collections were inadequate; physical facilities were substandard; staff, in too many cases, were poorly trained; and interlibrary cooperation, where it existed, was largely a local phenomenon. The substantial investment being made in biomedical research and the resulting new knowledge was threatened by an inadequate library mechanism for storage and retrieval of information.

Realizing that much of the value of the ever-increasing volume of knowledge created in the health sciences might be lost unless immediate measures were taken, the Congress authorized the National Library of Medicine (NLM) to initiate programs for library improvement, and for information research and development. The Act contains authorities for supporting projects to improve and extend library resources, to develop a Regional Medical Library system, to undertake communications research and development, to train needed personnel, and to provide critical reviews and other health science publications. The Act has enabled the National Library of Medicine to serve as a focal point in the Nation for coordinating and guiding efforts to improve health information access and utilization.

The results of the Medical Library Assistance Act are impressive. Through library resource project grants, new services have been implemented at academic medical centers and other major health institutions. Resource improvement grants have assisted libraries in hundreds of hospitals and other local health facilities. Research grants have supported the development of new techniques for library systems. Training grants have produced a new generation of capable individuals to provide the human resource in the academic health institutional and hospital libraries. These results have been further magnified by the Regional Medical Library Program: a nationwide efficient library network comprising seven Regional Medical Libraries, some 100 resource libraries in academic medical centers, and more than 3,000 libraries in hospitals and other health-related institutions. Through programs of library cooperation and resource sharing, this network provides health professionals, regardless of their location, convenient access to NLM's online computerized reference services, and to the books, journal articles and audiovisual materials they require.

Although the health library community is well along in establishing a foundation for a national library network which is responsive to needs of all health workers, much is still to be done. Many smaller health institutions, in the aggregate serving large numbers of professionals, are without adequate library resources and services. Not all health institutions are linked with the Regional Medical Library Network. Some libraries are still lacking a full range of services, and have not benefitted from modern communications technology. MLAA programs should continue to provide needed support for these libraries.

Grants to support research in better methods to organize, distribute, and use medical information were also provided. In recent years, some of this support has been channeled to support research and training in medical informatics. In addition to funding grant proposals from individual investigators, NLM has supported five program project grants at major institutions to investigate various aspects of computer technology applications for improving the dissemination of health information. The projects deal with such subjects as artificial intelligence, clinical problem-solving, and the development of medical databases.

Another aspect of the computers-in-medicine program has been support for training talented individuals to apply computer technology to problems in the health sciences. This training program was begun in 1972, after a study revealed that the original training program for health-science librarians had been successful in alleviating the nationwide shortage of qualified biomedical librarians. In the last 10 years, some 350 professionals have undergone doctoral level training in the field of medical informatics. Although a modest number, it represents a cadre whose influence will be multiplied as they move into responsible positions in medical centers. There remains a great need for such professionals in academia, industry, and government.

Improved biomedical communications are essential if the Nation is to exploit the findings of health research in the advancement of medical education, practice, and continued research. The Medical Library Assistance Act programs are the unique focal point for a national, coordinated effort to make the full range of health knowledge available to all.

The CHAIRMAN. Thank you, Dr. Cummings. We appreciate that. I also have been very interested, Dr. DeVita, in the computer approach that you are taking to the dissemination of information with regard to all aspects of cancer. I think you have made some tremendous strides there, and I am interested in getting out there and taking a good look at that.

Dr. DEVITA. We owe a vote of thanks to the National library of medicine, Mr. Chairman, because they have been helping us quite a bit in getting this system up. We are quite excited about it, too.

The CHAIRMAN. How many areas of the country have access to your information?

Dr. DEVITA. Right at the moment it is in two phases. PDQ is the name of the system. PDQ–I is accessible through the 1,800 terminals through the National Library of Medicine that Dr. Cummings was referring to. PDQ–II we hope will be available through the computer industry itself, so it can be made available to a larger number: The AMA is very much interested in the system, and they hope to put it up on their Telenet service.

The CHAIRMAN. So they can bring it into each doctor's office who wants to work with cancer problems?

Dr. DEVITA. Through their office equipment, yes.

The CHAIRMAN. As I understand it, you provide information on every state-of-the-art aspect of cancer diagnosis and treatment on the PDQ. You expect by this summer to have PDQ–II?

Dr. DEVITA. We expect to be able to have the system up by this fall and at the National Cancer Advisory Board, announce some national mortality goals for bringing mortality down and survival up to the national average or, at the very least, to the state of the art in cancer treatment.

The CHAIRMAN. Virtually all universities in this country have access to PDQ under the present system?

Dr. DEVITA. Yes, indeed.

The CHAIRMAN. Now you want to make it available to every doctor who is interested in working with cancer problems?

Dr. DEVITA. Yes it will be available in a user-cordial format so that it is very simple to use and will not require computer skills to work with the system. That will make it more attractive, we think.

The CHAIRMAN. Dr. Cummings, I would like to ask you one other question that I think is important. It has come to my attention that there is a bioethics library and information retrieval system currently housed at the Joseph and Rose Kennedy Institute at the Georgetown University. This has been partially funded by your own extramural program, but I understand that this support is in jeopardy because of budget cuts. Now, if the Medical Library Assistance Act is funded as we recommend, at the $10 million level for fiscal year 1984, could you insure that this bioethics library will receive sufficient support?

Dr. CUMMINGS. Mr. Hatch, the library has supported the Kennedy Bioethics Institute at Georgetown for approximately 8 years. The total support amounts to approximately $900,000. We, in addition to supporting the creation of a published bibliography in bioethics, run a computer program for the Kennedy Institute, which makes available information on bioethics to all of the people who have access to our system. The library believes that its support has really run its normal course, but I do not wish to say that the funding for the institute is being stopped solely because of a lack of budget.

I think if a new application were submitted, it would have to receive a new review as a continuation of a long-standing grant. I understand that other institutes at NIH have joined together, making available to us additional funds for support of the Kennedy Institute through a multifunded venture, and this, I believe, will carry that program for 1 or 2 more years.

The CHAIRMAN. Thank you. I certainly appreciate all of you gentlemen being with us here today, and I want to personally give you my support and tell you how much we appreciate what you have done and what you are doing at the present time. We want you to know that the committee is open to you, and we hope that we can serve you even better in the future. We have a lot to learn here also, but this is one of the most enjoyable and, I think, important efforts that this whole committee undertakes. We appreciate all the effort you have put forth. We will try to get committee members out there on a site visit so that we become even more conversant with what you are doing. I think this will be the first time the committee has done anything like that. So if you will cooperate and help us in that, we would appreciate it.

Dr. WYNGAARDEN. We would be delighted.

The CHAIRMAN. Thank you very much.

[Additional questions submitted by Senator Hatch and Senator Dodd with responses from the panel follow:]

Questions for Dr. Brandt

from Senator Hatch

Dr. Brandt, I would like to ask several questions of the Administration regarding concerns we raised during the last Congress related to NIH. As you know, we conveyed these concerns in the Committee Report accompanying S. 2311. In lieu of multiple questions, I would appreciate your providing a brief written response to each section of this report relative to NIH. This would give the Committee an update on progress made to address these concerns. Could you provide this report, Dr. Brandt?

(See attachments)

"recent publicity regarding poor management and fraud among scientists whose research is supported by NIH" (p. 11, Senate Report 97-461)

A PHS task force to look into this issue developed a statement of general PHS policies and principles, which the Secretary has recently signed. This document provided two policy statements:

- It is the policy of the PHS to maintain high ethical standards in research and to investigate and resolve promptly and fairly all instances of alleged or apparent misconduct.

- The scientific community is expected to make every effort to prevent misconduct. Also, for every incident of alleged or apparent misconduct which is judged to warrant investigation by an awardee institution, that institution is expected to report on the matter to the head of the appropriate PHS agency/office or that agency's/office's designee in accordance with PHS reporting requirements.

Possible sanctions for misconduct, depending upon the severity of the case, were also included as follows:

- actions with respect to present or future grant and/or contract awards (e.g., imposition of special conditions, termination, recommendation for debarment or suspension);

- regulatory actions (e.g., disqualification);

- o in the case of intramural research programs, termination of employment or other disciplinary action.

In addition, responsibilities for action were assigned as follows:

- o The NIH Associate Director for Extramural Research and Training was designated as the PHS official responsible for developing, assessing, overseeing, and coordinating relevant policies and procedures.

- o Agency heads were assigned to ensure apropriate implementation of policies and procedures to make decisions about appropriate sanctions to be applied, and to designate appropriate officials within the agency to handle matters related to misconduct in science.

The PHS committee is currently working on more detailed procedures for awarding agencies, regulatory components, and intramural research programs, as well as more formalized processes for information sharing and joint investigations.

"persistent allegations that the peer review system is inefficient and sometimes unfair, in spite of multiple efforts in recent years to evaluate and improve the system" (p. 11, Senate Report 97-461)

The peer review system has responded to unprecedented demands by the scientific community by processing and reviewing increased numbers of applications over the period of the seventies and early eighties. The Division of Research Grants (DRG) has central operational responsibility for most of the system. The DRG currently operates 63 regularly chartered study sections comprised of more than 1100 members. In addition, it manages the Special Study Section, which conducts customized reviews of applications not appropriately reviewed in regular study sections.

As resources necessary to award grants in proportion to the application rate have dwindled, changes have occurred in the behavior of the peer review system, as well as in the applicant community, although a cause and effect relationship remains to be proven. Some of these changes are:

a. The rate of recommendations for approval for new research project applications increased from 62 percent in 1972 to 80 percent in 1982. The comparable rate for competing continuation applications has increased from 86 percent to 96 percent over the same period.

b. The award rate for these applications has decreased over the same period from 52 percent to 28 percent in the case of new applications and from 68 percent to 48 percent in the case of competing continuation applications.

c. Median priority scores for all competing research project applications recommended for approval have increased (become poorer) from 217 in 1972 to 225 in 1982, while those for applications actually awarded have decreased (improved) from 186 in 1972 to 159 in 1982.

d. The number of investigators seeking R01 grant support for the first time continues to increase. For instance, in 1980, there were 3081 first-time applicants as compared to 1744 in 1970.

As the number of unfunded applicants has mounted, criticisms leveled at the peer review system have intensified. The two principal criticisms are that the same people continue to serve as study section members and that study section members are not as well qualified as they were in the past. Actually, about 85 percent of all study section members are serving their first appointment at any one time. Further, priority scores and approval rates for study section members' applications are both very much better than those of the general applicant population.

New principal investigators (PIs) on NIH R01 projects continue to enter into the NIH research grant support system at an average annual rate greater than 10%. In the past five years the entry rate has averaged over 12%. Nearly a third of all competing PIs awarded each year are new; more than half of all new projects awarded each year are to scientists supported for the first time as principal investigators on NIH research grants. In fact, new applicants seeking support for their research as PIs on new research projects succeed at rates greater than other applicants who have applied previously.

These statistics belie the argument that the peer review system perpetuates the continued support of a select group of repeat investigators. Indeed, the facts substantiate that the system is coping very effectively with an increasing number of applications. However, despite all precautions, some inequities may occur. For this reason, in 1980 NIH established a formal procedure for handling commentaries and rebuttals to peer reviewers' evaluations. Another procedure used to strengthen the system is to convene a special review group for the occasional application that concerns an area of science not well represented on any study section.

"increase in indirect costs . . . and an Administration proposal that indirect costs be cut 10 percent across the board" (p. 11, Senate Report 97-461)

"the Committee expects the Department to renegotiate [indirect cost] rates on an institution-by-institution basis" (p. 73)

As a consequence of the directive in this Report and directives from the Appropriations Committees, NIH will reimburse indirect costs in full in FY 1983.

In addition, NIH and PHS officials have consulted with the research institution community in developing a report to be submitted shortly to the Appropriations Committees. The report will make a number of alternative recommendations for dealing with the question of indirect cost reimbursement.

The recommendations include the following:

- o Fixed-allowance reimbursement, based on the historical indirect cost/total cost level for each institution
- o Across-the-board reduction in indirect costs
- o Redefinition of reimbursable indirect costs
- o Establishment of a standard fixed allowance
- o Choice of a fixed allowance or a negotiated rate, for each institution.

"inadequate research in preventive medicine and health promotion" (p. 11, Senate Report 97-461)

Current NIH expenditures for prevention research are listed below.

PREVENTION RESEARCH
(Dollars in thousands)

	1980 Actual	1981 Actual	1982 Actual	1983 Estimate	1984 Request
Cancer......................	$123,179	$127,454	$132,869	$ 94,845 1)	$ 98,639
Heart.......................	117,072	120,707	121,705	124,000	125,500
Dental......................	6,921	6,267	6,878	7,703	8,627
Arthritis...................	17,710	19,438	28,474 2)	32,000	32,500
Neurology...................	25,101	27,664	29,907	33,257	37,362
Allergy.....................	27,480	32,948	30,345 3)	35,758	37,183
General Medical Science....	6,041	5,705	2,728 4)	2,750	2,800
Child Health................	85,373	86,710	94,958	108,800	112,100
Eye.........................	29,612	31,263	36,537	40,884	42,151
Environmental Health.......	45,754	54,390	82,582 2)	137,954 1)	142,421
Aging.......................	13,502	16,340	17,650	20,451	20,610
Research Resources.........	6,539	10,086	14,670	16,822	18,175
Fogarty.....................	2,175	3,444	3,249	3,573	3,864
TOTAL, NIH..........	$506,459	$542,416	$602,552	$658,797	$681,932

1) Transfer of National Toxicology Program to NIEHS from NCI - $47,988.
2) Increase over 1981 reflects a re-evaluation of reportable prevention efforts, which has resulted in an increase of funds reportable for prevention research.
3) Reduction in collaborative intramural program.
4) Iatrogenic diseases are no longer included as prevention research.

Prevention research, for the purposes of this table, includes intervention before the biologic onset of the disease in question (e.g., reduction of dust levels in occupational settings), basic research directly relating to development of preventive measures, and direct preventive measures themselves (such as vaccination programs, regulatory activities, and public education).

Included also are epidemiologic studies allowing for the identification and quantification of risk factors relating to personal characteristics such as habits associated with diet, use of cigarettes, alcohol consumption, exercise, and the like. Also included is the treatment of various biological conditions and risk factors such as elevated cholesterol and blood pressure levels and cigarette smoking to prevent cardiovascular complications such as myocardial infarction and stroke as well as chemoprevention, where there is a population with disease but not frank carcinoma that is being treated with chemoprevention (e.g., patients with leukoplakia being treated to prevent oral squamous cell carcinoma).

"disproportionate funding of rare diseases processes (p. 11, Senate Report 97-461)

Research in rare diseases, as in all other areas, is predicated upon basic scientific opportunities, and the funding of particular studies is dependent on the excellence of the proposals. In the case of many rare diseases, an insufficient understanding of the underlying mechanism of disease often exists and not as many scientific opportunities exist as we would hope.

At the level of basic research, the eventual application of findings to a particular disease cannot be foreseen, yet it is precisely through our funding of fundamental research that advances have been made in several important rare diseases.

For example, significant advances have been made in the past 3 to 5 years in the understanding and treatment of myasthenia gravis. While the etiology of this disorder is not yet fully known, studies in fish have helped scientists to elucidate the way in which nerves tell the muscles to contract. These findings, coupled with new information on basic immunology, have allowed scientist/physicians to develop hypotheses which are leading to a better understanding and treatment of the condition.

In the area of developing drugs to treat rare diseases, NIH is primarily involved in anticancer drugs, vaccines, anticonvulsants, and antiviral agents. In FY 1983, it is estimated that about $68 million will be allocated to developing drugs to treat rare diseases; about $48 million of that will be devoted to development of anticancer drugs.

"inadequate funding of research equipment, with a rapidly growing obsolescence of scientific instrumentation . . ." (p. 11, Senate Report 97-461)

"The Committee . . . encourages HHS to examine possible solutions . . . which might aid in alleviating this significant problem" (p. 13)

Currently, the NIH research project system provides for relatively inexpensive equipment that does not lend itself to shared usage; shared instrument grants provide medium-priced instruments that are shared on an institutional basis. For example, to meet the needs of research projects of interest to the National Institute of General Medical Sciences (NIGMS), instrumentation which can be used by a group of investigators is provided for some NIH grantees (at least half of whom must be NIGMS grantees) through a shared instrumentation program. In addition, the Division of Research Resources (DRR) provides for shared instrumentation through institutional awards to qualified grantees. In FY 1982, a total of about $5 million was allocated for shared instrumentation; expenditure of $16 million is estimated for FY 1983. The purchase of shared instrumentation is also possible under a DRR Biomedical Research Support Grant.

In addition, the DRR Biotechnology Resources Program is set up to assure development and availability of high-technology instruments so costly that they must be shared on a regional or National basis. In FY 1982, about $20.3 million was allocated for this program ($15.3 million from DRR); about $36.4 million is estimated for FY 1983 ($20.4 million from DRR).

A pilot series of co-funded program project grants (funded by DRR and the appropriate categorical Institute) is now being considered by NIH as a means of fostering combined sources of support for categorical instrumentation needs.

NIH recognizes the seriousness of this problem and is looking into the most efficacious means of solving it, including consideration of the value of cost sharing with other Federal agencies or with industry.

"increasing competition and friction among scientists and lay advocates of specific disease or organ system research programs, who seek for targeted funding, or specific legislative emphasis" (p. 11, Senate Report 97-461)

NIH is also increasingly concerned about this situation. Over the past 10 years, there have been over ten legislative proposals to establish new NIH Institutes, and numerous proposals to set aside funds or otherwise to place special emphasis on certain programs related to specific diseases or systems of the body. The unfortunate consequence of these mandates is to limit increasingly the ability of NIH to support a broad range of research projects directed not at narrow and isolated components of public health, but at the whole spectrum of activities designed to understand, prevent, and treat disease.

Legislation recently introduced in the House (H.R. 2350) exemplifies this problem by requiring specific earmarks of funds or special emphasis or activities for

- Health Promotion and Disease Prevention Centers;
- Cancer Centers;
- Kidney and urologic diseases research centers;
- Research in spinal cord regeneration;
- Operation of the National Center for Health Care Technology;
- Sickle cell disease centers;
- Pertussis vaccine study;
- Study of personnel for health needs of the elderly;

- Study of commercial use of biomedical research results;
- Interagency committee on learning disabilities;
- Research into diet therapy in the treatment of end-stage renal disease;
- Research in the relationship between diet and cancer;
- Research in developing research methods that reduce the use of animals or minimize animal pain;
- Mental retardation centers;
- National Commission on Orphan Diseases.

"ineffective coordination and cooperation among some Institutes at NIH and other federal Agencies conducting related health research projects" (p. 11, Senate Report 97-461)

The NIH has developed a variety of mechanisms for achieving coordination of biomedical research activities and promoting effective collaboration. For example,

- Disease prevention has been identified as a major Departmental initiative, and the NIH has assumed an active role in implementing this initiative by establishing a position of Special Assistant to the Director, NIH, for Research Related to Disease Prevention to work with the NIH Institute Directors in developing a coordinated program. To assist in this program, a trans-NIH committee was established to provide a strong link between the Office of the Director, NIH, and the Institutes in identifying and coordinating opportunities in disease prevention and relating the NIH effort to the overall Department initiative.
- In response to growing concerns about the health effects of chemical agents in the environment, the Secretary, DHHS, established the National Toxicology Program (NTP) to: (1) integrate DHHS activities to permit the most effective use of resources, (2) consolidate existing expertise, and (3) establish a dialogue between the research and regulatory agencies. The activities of the NTP are planned and conducted under the leadership of a Program Director who is also Director of the National Institute of Environmental Health Sciences. In addition to the relevant PHS agencies and regulatory organizations, various industry

associations, public interest groups, and members of the scientific community actively participate through membership on a Board of Scientific Counselors, through public peer review of Technical Reports and an Annual Plan, and through attendance at public meetings.

- The Interagency Radiation Research Committee was established in response to legislation (P.L. 95-622) directing HHS to "establish a comprehensive program of research into the biological effects of low-level ionizing radiation" and "conduct a comprehensive review" of Federal research programs on the biological effects of ionizing radiation. It was the intent of Congress that this review also coincide with the development of a comprehensive Federal strategy for future research in this area.
- Many of the NIH Institutes have assumed primary leadership responsibility for coordinating activities in agency-wide areas of research. Through such mechanisms as, for example, the Diabetes Mellitus Interagency Coordinating Committee, the Arthritis Interagency Coordinating Committee, and the Cystic Fibrosis Coordinating Committee, the research, research training, data collection, and information transfer activities of the agencies are dealt with in a coordinated fashion.
- Within the NIH a wide variety of trans-NIH coordinating committees have been established to identify areas of mutual interest, to develop joint program announcements, and to share in the development of workshops, conferences, and symposia designed to identify areas of research need and to stimulate research in areas of highest priority. One highly successful example of this is the NIH Nutrition Coordinating Committee.

In addition, NIH Institutes are involved in many informal collaborative activities and participate in many interagency agreements designed to facilitate biomedical research.

National Institute on Aging

"Transfer of the Laboratory of Neurosciences to . . . Bethesda" (p. 12, Senate Report 97-461)

In FY 1982 the Institute's Laboratory of Neuroscience established a clinical research program at the Warren G. Magnuson Clinical Center at NIH, with use of a six bed patient care unit. The basic research program of the laboratory will be relocated from the Gerontology Research Center in Baltimore to the Clinical Center at NIH this coming summer. Location of the total program at NIH will greatly facilitate our overall research efforts in the areas of the dementias and neurosciences and will facilitate collaborative efforts with the intramural program of the other institutes. This laboratory will examine changes in the normal brain with age and the dementias, and such areas as cerebral metabolic changes. For example, glucose metabolism is one of three major interrelated measures of brain activity--the other two being brain blood flow and oxygen consumption. NIA investigators have found no significant age-related alterations in brain glucose metabolism. These studies suggest that the healthy aged brain is as active and efficient as the healthy young brain. Future studies will continue to build upon and analyze the results of this work, and will lay the groundwork for research on various pharmaceutical approaches in the treatment of the dementias.

Aplastic anemias and Fanconi's anemia (Page 17, Senate Report 97-461)

Aplastic anemia is most commonly acquired but there are patients with a genetic predisposition to bone marrow failure who are said to have "constitutional" aplastic anemia. Fanconi's anemia is perhaps the most commonly reported congenital aplastic anemia. There have been slightly more than 300 cases cited in the literature and new cases are being added to the list as a result of a recently inaugurated International Registry, located at the Rockefeller Institute. In contrast, almost 3,000 deaths per year are due directly or indirectly to acquired forms of aplastic anemia.

Patients with Fanconi's anemia are born with characteristic organ and bone abnormalities. The inheritance pattern is autosomal recessive and the gene frequency of the heterozygote is calculated to be approximately 1/300. An interaction of the Fanconi's anemia gene with the environment has been suggested by reports of the simultaneous onset of aplastic anemia following a viral illness.

Most patients die before the age of 25 and only 50% survive for 5 or more years after diagnosis. Androgens are helpful in about half the cases, and they prolong life by as much as 5 years. Bone marrow transplantation, if done early, may hold promise for future treatment. However, results to date have been disappointing, in part, it is believed, because of the use of cytoxan to prepare the patient. This agent apparently leads to bone marrow damage which compromises the transplant. New approaches to transplantation, however, appear to be more promising.

Several Institutes at the NIH provide extensive support for normal hematopoiesis research but, in light of recent scientific advances, more research directly related to aplastic anemia would be desirable. In an effort to stimulate and support more research in this important area, the Division of Blood Diseases and Resources issued a Request for Applications (RFA) entitled, "Etiology, Pathogenesis, and Treatment of Aplastic Anemia." Fanconi's anemia is specifically highlighted in this announcement. We have received 45 letters of intent to submit a proposal for the April 15, 1983, receipt date. We anticipate making about five awards on September 30, 1983.

In addition to this RFA, the NHLBI has organized an international conference on aplastic anemia which will be held June 26-28, 1983, at Airlie House in Virginia. The National Institute of Arthritis, Diabetes, and Digestive and Kidney Diseases, the Fogarty International Center, and the University of Washington will cosponsor this meeting which is intended to bring together clinicians and basic scientists to discuss recent laboratory and clinical advances related to aplastic anemia.

Coordination of hematologic research within the NIH. (Pages 16, and 17, Senate Report 97-461)

Hematologic research at the NIH is distributed among a number of Institutes, but is largely focused in the National Heart, Lung, and Blood Institute, the National Institute of Arthritis, Diabetes, and Digestive and Kidney Diseases, and the National Cancer Institute. Research programs of these three Institutes are well coordinated and the red cell and bone marrow interests of NHLBI and NIADDK complement each other.

Hematologic research at the NIH is coordinated through several committees which provide formal channels for communication. Through this mechanism, overlapping programs are avoided and activities which might fall "through the cracks" are reviewed.

The committees are as follows:

A) Intra-NIH Coordinating Committee for Blood-Related Activities.

The function of the Committee is to serve as a principal mechanism for coordinating and integrating blood and blood-related research programs conducted or supported by the NIH.

The membership of the NIH Coordinating Committee for Blood-Related Activities represents eight major components of the NIH. NHLBI is the lead agency for this Committee and the Director, Division of Blood Diseases and Resources, has been delegated the chairmanship by the Director, NHLBI.

B) Interagency Technical Committee (IATC) - Working Group on Blood Resources.

The goal of the IATC Working Group on Blood Resources is to examine and coordinate Federal research activities which concern blood and its substitutes, which are designed to reduce disability, morbidity, and mortality from diseases or conditions for which whole blood, its components or substitutes, provide preventive or curative treatment.

Memberships include most Federal agencies with programmatic interests in blood resources. In addition, representatives of a number of professional societies, blood bank associations, and health foundations are invited to participate in these meetings.

C) Sickle Cell Disease Advisory Committee.

This Committee was established by the Secretary of HEW on May 9, 1971, to advise the Secretary on the Sickle Cell Program, to suggest priorities within the Program, and to make recommendations on matters pertaining to planning, implementing, and evaluating various aspects of sickle cell disease. The Committee reviews activities across Federal agencies to avoid unnecessary overlap.

Membership consists of seven health care delivery representatives, four prominent lay leaders, and a number of ex officio members.

Finally, grant referral guidelines published and periodically revised by the NIH Division of Research Grants help to ensure appropriate assignment of hematologic research grant applications to relevant NIH institutes.

Coordination of lung research within the NIH and other government agencies. (Page 17, Senate Report 97-461)

The Interagency Technical Committee (IATC) coordinates those aspects of all Federal Health programs and activities relating to heart, blood vessel, lung, and blood diseases and blood resources to assure the adequacy and technical soundness of such programs and to provide for the full communication and exchange of information necessary to maintian adequate coordination of such programs and activities.

The IATC, which is comprised of seventeen Federal agencies, including the National Heart, Lung, and Blood Institute, meets at least twice a year. In 1982, the IATC devoted its September meeting to discussions on research in pulmonary diseases. Two major scientific presentations were made to the Committee. Dr. Carol Vreim, Chief of the Interstitial Lung Diseases Branch, Division of Lung Diseases, NHLBI spoke on the syndrome known as primary pulmonary hypertension and described current research efforts and the Division's recently initiated patient registry designed to collect and evaluate data on patients with the syndrome.

Dr. Thomas Hodous of the National Institute on Occupational Safety and Health (NIOSH) described the pulmonary disease research program supported by the NIOSH and discussed in detail current understandings and research activity on occupational lung diseases including byssinosis, coal miners pneumoconiosis, and chronic bronchitis among cement workers.

The IATC also makes available to its members current listings of federally-sponsored research projects in heart, blood vessel, lung, and blood diseases and blood resources. These listings have encouraged interagency cooperation and coordination.

Recently, the NIH Director also announced that the National Institute of Arthritis, Diabetes, and Digestive and Kidney Diseases (NIADDK) will have lead responsibility for coordinating cystic fibrosis (CF) research at NIH. Co-chairing the NIH CF Coordinating Committee are representatives from NIADDK and NHLBI.

No addditional administrative costs were engendered for these efforts.

"Nutrition may play a pivotal role in the development of many diseases, including our most debilitating and costly chronic diseases, and the Committee feels it is in the best interest of our citizens to encourage all institutes to emphasize and enhance nutrition-related research relevant to the respective disciplines. One noteworthy example of much needed research relates to nutritional therapy of patients with chronic renal disease. Previous studies suggest renal failure can be substantially retarded by such treatment, and if implemented on a large scale could result in considerable savings to the Federal End Stage Renal Program." (Senate Report No. 97-461, p. 12)

The National Institute of Arthritis, Diabetes, and Digestive and Kidney Diseases shares the Committee's interest in nutrition research, as it relates to kidney disease. In Fiscal Year 1982, the Institute supported about $4 million in research related to the broad area of nutrition and kidney disease. In April of 1982, we supported a conference on nutritional therapy and chronic renal disease. The Institute has also supported pilot studies to determine patient compliance with low protein diets, and has directed approximately $7 million to a 6-year national cooperative dialysis study, which included assessment of nutritional parameters. Most recently the institute has developed two new initiatives, which it plans to begin in Fiscal Year 1984. These initiatives will involve studies of (1) the natural history and progression of the diseases leading to end stage renal disease and (2) identifying quantitative indices for initiating dialysis. Investigation of nutritional variables will be an inherent and important part of both of these initiatives.

"The Committee expects the Secretary to report back to the Committee on the effect of the NIADDK restructuring, and to evaluate the degree to which the restructuring has addressed the perceived inequities." (Senate Report No. 97-461, p. 17)

The National Institute of Arthritis, Diabetes, and Digestive and Kidney Diseases (NIADDK) was elevated to a bureau of the National Institutes of Health in April 1982. In his report to the Committee on S. 1939, legislation introduced in the 97th Congress to create a separate institute for arthritis and musculoskeletal diseases, former Secretary Schweiker commented on the benefits of the NIADDK having achieved bureau status. Assistant Secretary for Health, Edward N. Brandt, Jr., also reported in this regard at hearings held on this bill by the Committee in July 1982.

Essentially, bureau status has helped NIADDK leadership to improve managerial effectiveness and to enhance NIADDK relationships with advisory and constituent groups. With respect to perceived inequities, bureau status has largely enabled NIADDK to begin a new budget allocation process which permits each division to participate more directly and fully in budgetary decisions and to have greater flexibility in allocating funds among its respective programs. This process is also geared toward greater consultation with concerned health voluntary and professional groups and toward making more equitable allocations among divisions. The arthritis community--the Arthritis Foundation, the National Arthritis Advisory Board, and other groups--is now participating fully in NIADDK budget discussions. The Arthritis Division has clearly benefitted from this new approach, and was the only NIADDK component which did not absorb a portion of the $1 million loss NIADDK incurred in Fiscal Year 1982.

Other advantages of bureau status are:

- Increased public visibility for the Department's national research effort in arthritis, diabetes, digestive diseases and kidney diseases.

- Establishment of a more effective organizational structure for improved management of these high-priority national programs.

- More highly focused responsibility for the national research efforts in arthritis, diabetes, digestive diseases and kidney diseases, and other specialized areas.

"A need (exists) to coordinate research conducted in skin diseases throughout the National Institutes of Health, as well as the National Institute for Occupational Safety and Health." (Senate Report No. 97-461, p. 18)

Coordination of skin diseases efforts at NIH and throughout the Federal Government is being enhanced through an ad hoc interagency dermatology working group. To date, this group has met three times, and a fourth meeting is planned during 1983. The chairman of the group is the Skin Diseases Program Director, National Institute of Arthritis, Diabetes, and Digestive and Kidney Diseases (NIADDK). The working group includes representatives from the National Institute of General Medical Sciences; the National Heart, Lung, and Blood Institute; the National Institute of Allergy and Infectious Diseases; the National Cancer Institute; the National Institute on Aging; the National Eye Institute; the National Institute of Neurological and Communicative Disorders and Stroke; the National Institute of Environmental Health Sciences; the National Institute of Dental Research; the Division of Research Resources; the HHS Division of Nursing; the Food and Drug Administration; the Veterans Administration; and the National Institute of Occupational Safety and Health. Objectives of the working group include:

- To provide up-to-date information on funded research projects within the various institutes and agencies.

- Identify gaps in under-supported areas of research within the field of skin disease related problems.

- Identify common interests within the area of skin-disease related research; that is, areas of interest to more than one institute or agency.

- Coordinate Federal activities in skin disease related research.
- Aid in the proper assignment and referral of applicants and applications related to skin diseases.
- Aid in the search for funding of important projects.
- Stimulate new research and research initiatives within skin diseases.
- Develop reasonable, accurate financial estimates for the support of skin-disease related research and in particular for some of the subgroups within that broad category.

The working group has been guided in its work by the 1979 NIADDK-supported evaluation study, "Analysis of Priorities and Needs for Research in Dermatology." As requested by the House and Senate Appropriations Committees, the Institute is currently in the process of updating this analysis, and expects to have a revision available at the appropriations hearings on the Fiscal Year 1985 budget.

"The Committee has heard of considerable concerns expressed by the digestive diseases research community regarding inadequate epidemiological data. Insufficient attention to such research related to digestive diseases is unfortunate in view of the prevalence and disability associated with these illnesses." (Senate Report No. 97-461, p. 18)

The National Institute of Arthritis, Diabetes, and Digestive and Kidney Diseases (NIADDK) recognizes and shares the Committee's concern regarding the need for epidemiologic data in digestive diseases research. Currently, the Institute is developing a proposal for a digestive diseases epidemiology and data system program. This proposal is being formulated by a gastroenterologist and data system expert from Johns Hopkins University, who is in consultation with other experts in the field. It is expected that the NIADDK program will pursue cooperative epidemiology initiatives with other organizations. The Institute is already working with the National Center for Health Statistics (NCHS) on a project to determine the prevalence of gallstone disease in subjects participating in an NCHS study of Hispanic Americans. In addition, efforts will be made to employ data obtained from endoscopic studies as a model of a data system in archive. This project will be pursued this summer under the aegis of the American Society for Gastrointestinal Endoscopy.

The Institute has also promoted a workshop which considered diagnostic criteria for functional bowel disease. Studies to arrive at precise definitions for this condition are under way. Interested investigators are applying the criteria developed at the workshop under field conditions in order to arrive at a practical and standard basis for diagnosis.

The Institute recently issued a solicitation for exploratory grants for digestive diseases research centers. These centers will provide a unique opportunity to gather epidemiologic data and to study populations with digestive diseases. Institutions having an interest in expertise in the epidemiology of digestive diseases are able to submit applications under this announcement. The Institute welcomes and encourages work in epidemiology and recognizes that this field needs nurturing.

"Advocates for patients suffering from digestive disorders, as well as the research community, have recommended establishing research centers similar to those which have proven successful in facilitating research in other specific health problems, i.e., cancer centers, arthritis centers....The Committee recommends NIADDK consider development of such centers supporting digestive diseases research as recommended by the Digestive Diseases Advisory Board, with consideration of resources available and continuation of funding the recommended level of research grants." (Senate Report No. 97-461, p. 18)

Recognizing the interest of the Congress, the research community, and the Digestive Diseases Advisory Board in the establishment of digestive diseases research centers, the National Institute of Arthritis, Diabetes, and Digestive and Kidney Diseases (NIADDK), published a solicitation for exploratory grants for such centers in February 1983. The solicitation is provided for the record.

The objective of the exploratory grant is to provide partial funding for the cost of planning and developing a high quality digestive diseases center. The special receipt date for submission of applications is May 16, 1983, with the earliest funding date being September 26, 1983. Successful exploratory grant applications will be funded in amounts not to exceed $25,000 in direct costs for a 12-month period.

The digestive diseases centers will be charged to develop and conduct basic and clinical research into the cause, diagnosis, early detection, prevention, control and treatment of digestive diseases and related physiological, pathophysiological, congenital or metabolic disorders resulting from such diseases. The planning phase of the grant may consist of but is not limited to:

- Departmental and interdepartmental planning to integrate a broad spectrum of digestive disease related activity;

- Planning the establishment of specialized resources and facilities;

- Feasibility surveys to identify appropriate patient populations, identify special problems and opportunities, etc.

- Use of consultants to solidify plans for center activities and resources.

The NIADDK expects this initiative to enhance research efforts in digestive diseases, and is pleased to respond administratively to Congressional interest in this area.

Question: Dr. Brandt, I understand that the Administration is generally supportive of S. 773, the Biomedical Research Bill we are considering today. However, I am fully aware that the Administration is not supportive of the proposed National Institute of Arthritis, Musculoskeletal and Skin Diseases. You have previously cited concerns about administrative costs, and setting a precedent for the creation of multiple new institutes. How can you justify these concerns, given that much of the expertise and resources for the proposed institute are already in place in the National Institute of Arthritis, Diabetes, and Digestive and Kidney Diseases, and we have requested, in statute, a careful study of the NIH administrative structure to be conducted before additional institutes are created?

Answer: We estimate the administrative cost for establishing a separate institute for arthritis, musculoskeletal and skin diseases at $4.8 million. This estimate is based on the actual fiscal year 1981 administrative costs incurred by two comparably sized institutes at the National Institutes of Health and is, in our view, a very realistic estimate. Sixteen positions--representing approximately $800,000--could be transferred from the National Institute of Arthritis, Diabetes, and Digestive and Kidney Diseases (NIADDK) to the proposed new institute for arthritis, musculoskeletal and skin diseases. The net administrative costs of the new institute would therefore be approximately $4 million.

Although it has been suggested that NIADDK could transfer more than $800,000 to a new institute, this would not be feasible. Currently, NIADDK has an extremely lean and efficient administrative apparatus which requires only approximately 4% of the total Institute's budget, an overhead rate which is already 20% less than the average NIH-wide administrative costs. This efficiency reflects the fact that most NIADDK administrative services are provided centrally to the Institute's ten program areas, including support services such as personnel management, program analysis, financial management, and grants management. If NIADDK were required to transfer more than $800,000 to the new institute, as provided for in S. 773, the research efforts and administrative management functions of the remaining programs in the parent institute including diabetes, digestive diseases and kidney diseases would be adversely affected. Ultimately, the lost resources would have to be restored, and the replacement costs would be attributable to creating the new institute for arthritis, musculoskeletal and skin diseases.

With respect to the provision in S. 773 that would require a study of the administrative structure of the National Institutes of Health (NIH), we agree this proposal is timely and desirable, and in fact have already initiated such a study administratively under contract with the National Academy of Sciences, Institute of Medicine. Clearly, one reason for this study is to place questions regarding the creation of new NIH institutes into an appropriate framework in which careful deliberation can occur before decisions are made that would substantially alter the organization of NIH. We believe, however, that a complete moratorium must be placed on the creation of any new institutes--including the proposed new institute for arthritis, musculoskeletal and skin diseases--pending consideration of the results of this study. Since the study currently under way by the Institute of Medicine will take a comprehensive and systematic look at the entire structure of NIH, it seems reasonable and desirable to consider the question of a separate arthritis institute in the context of that study.

As you know, there have been many proposals to transfer health-related activities in the Federal government to the NIH. I am concerned that the activities which proponents would like to be administered by NIH may not be appropriate for the research institute's mission. Could you please clarify for the Committee what you understand the role of our National Institutes of Health is and how we might better focus our legislative activities to accomplish their mandate?

NIH is distinct from the other Public Health Service agencies, all of whose missions relate to the health of the American people, because the primary mission of NIH is the conduct and support of biomedical research with the objective of the prevention, treatment, and cure of disease and disability. NIH does not provide health services other than therapeutic measures and care incidental to research. It is also not a regulatory agency.

Research conducted by other agencies can be distinguished from that of NIH by the relationship of each agency's particular kind of research to the mission of the agency. For example, the Food and Drug Administration's (FDA) research component supports FDA's mission to regulate food, human and animal drugs, and medical devices; the Centers for Disease Control, and its component, the National Institute of Occupational Safety and Health, conduct and support research on communicable and occupationally related diseases, in support of the mission to control the spread or limit the incidence of these diseases; the institutes of the Alcohol, Drug Abuse, and Mental Health Administration support research focused on these closely related problems, and which is inextricably linked with their public education activities; the National

Center for Health Services Research is responsible for economic and social research related to the provision of health services. None of the above activities is consistent with the NIH mission, yet at one time or other all of them have been proposed as potential NIH responsibilities. The danger in this is that when activities not directly related to research in understanding, preventing, and treating disease are assigned to NIH, the primary mission of the agency is diminished.

Legislation which reauthorizes expiring NIH programs is necessary to continuing this important research mission. Additionally, Congressional oversight and expressions of interest in various aspects of NIH management and programs has clearly been helpful. For example, it was Congressional interest which initially led to the decision to negotiate with the Institute of Medicine to conduct a study of the organizational structure of NIH. The study, which is now underway, is timely and appropriate. NIH is grateful for Congressional support for this activity.

Questions for Dr. Wyngaarden
from Senator Hatch

(Questions 1 and 2 are answered in the hearing transcript, pages 17-22 plus insert)

We receive literally thousands of letters from citizens and organizations who criticize NIH for allegedly not providing research funds to investigate diseases or treatments which are not deemed worthy of attention by the traditional scientists. These complaints often come from individuals who have suffered from serious diseases, such as cancer or chronic arthritis, and who have ardent testimonials about the benefit of a particular drug, diet, or medical device. Many elected officials and their staffs are impressed with the sincerity of these complaints and have asked me to apply pressure to the scientists and administrators at NIH to be more responsive. I understand that the majority of clinical research is conducted with rigid scientific methodology requiring double-blind comparisons for verification. However, is there a process at NIH whereby "unproven" or "alternative" treatments or diets, which have gained significant popular attention can be investigated in an efficient and economical fashion to determine if there is a basis for more thorough, traditional research regarding their efficacy? If this were possible, it would certainly help in responding to many of our citizens who, quite frankly, feel that our federal research effort is insensitive and unresponsive to their concerns.

It is important to distinguish unproven treatments from those about which we may not know a great deal but which offer promise. For example, many "folk remedies" that use plants have proven successful. Digitalis is a prime example. But in all of these cases, there has been some scientific basis for further study. When compounds appear to be effective in early studies, the Institutes vigorously pursue further research. However, it is a long process to go from early studies on animals to demonstrating the safety and efficacy of a drug or a treatment. We need to be extremely cautious in responding to anecdotal reports of treatments or cures.

Last summer, the Institute of Medicine (IOM) issued a report entitled "Health and Behavior: Frontiers of Research in the Biobehavioral Sciences." The report makes the point that today the heaviest burdens of illness are related to long-term patterns of behavior often referred to as "lifestyle."

According to the report, as much as 50 percent of mortality from the 10 leading causes of death in the United States can be traced to lifestyle.

Can you tell me what the National Institutes of Health are doing to investigate these behavioral causes of illness? How much of the total NIH budget is devoted to investigate the behavioral aspects of disease?

There is widespread interest among the NIH Institutes in research on behavioral factors in the causation and control of disease. In fact, NIH sponsored part of the IOM study which is quoted in this question and made major contributions to its completion. NIH has also played a major role in the conduct or support of the scientific research which the IOM reviewed in the course of its study. In the area of cardiovascular disease research, for example, the IOM report cites 48 original scientific articles published since 1970. The source of support is identified in 40 of these articles; 32 were either supported or conducted by NIH.

In order to ensure that grant applications in the field of behavioral medicine are reviewed by experts acknowledged for their leadership in the field, a new study section for behavioral medicine was established in 1980 in the Division of Research Grants. This is tangible assurance to investigators in the field that NIH intends to encourage development of new knowledge in this area. In addition, the National Cancer Institute, the National Heart, Lung, and Blood Institute, and the National Institute on Aging, which have legislatively mandated responsibility for community outreach and education regarding the diseases or conditions that are principally considered in the IOM report, have organizational units that specialize in behavioral medicine.

Among the many research programs that NIH is currently supporting that are germane to behavior as a determinant of disease are the following:

- The National Heart, Lung, and Blood Institute (NHLBI) supports three community intervention grants, one each in Rhode Island, Minnesota, and California, which are studying the efficacy of attempts to influence the lifestyle of whole communities so that risk factors for heart disease will be lessened. Long-range consequences in terms of cardiovascular morbidity and mortality are being followed.

- NHLBI supports six current research projects which involve interventions to assist people to stop smoking. These cover several sectors of the population including blue-collar workers, rural high school students, and persons in an out-patient clinic.

- Through preventive cardiology academic awards, NHLBI is influencing the teaching of medical students so that the next generation of physicians will be receptive to knowledge regarding behavior and lifestyle factors and utilize it in practice.

- While scientific knowledge about the relationship of behavior to the cause of diabetes is limited, there are important behavioral and psychological aspects of coping with the disease, such as maintaining a low body weight, exercising, and avoiding malnutrition. The National Institute of Arthritis, Diabetes, and Digestive and Kidney Disease (NIADDK) is currently supporting 18 grant projects with major components in these areas.

- The National Institute of Child Health and Human Develoment (NICHD) is active in supporting studies of the determinants of success in the breast feeding of infants and on the behavioral antecedents of cigarette smoking and other health-threatening habits in children. The Institute is planning to sponsor a conference on research methodology in studies of children's health behavior in 1983.

- The National Institute on Aging (NIA) is sponsoring both basic and applied research in exercise physiology in the elderly and on the role of physical fitness in reducing the risk of cardiovascular disease among older Americans.

- NIA is serving as lead Institute for a collaborative study between NIH and the National Center for Health Statistics to obtain follow-up information on 14,400 Americans who were carefully examined in a major health survey that lasted from 1971 to 1974. This study will make it possible to relate health outcomes to behavioral and other risk factors observed a decade ago and to learn how these characteristics have changed over time.

- The National Cancer Institute (NCI) has brought together a number of organizational units in the Smoking, Cancer, and Health Program. That program's objectives for the immediate future include evaluation of smoking cessation methods in industrial populations at unusually high risk of cancer because of concurrent environmental exposure, study of the role of "smokeless tobacco" promotion as a means of recruitment of young people to smoking, and evaluation of mass communications approaches to reducing prevalence of smoking.
- NCI has also recently undertaken a large-scale prospective study to examine the influence of lifestyle factors on cancer incidence.

These are only a few examples to illustrate the emphasis that NIH places on the examination of all aspects of disease, the sociocultural as well as the biochemical. NIH continues to work vigorously to sponsor and encourage research into the behavioral determinants of disease, and to explore the possibility of using this knowledge for practical applicantion in prevention and treatment of disease. In this regard, NIH works closely and in a coordinated fashion with the inherently more behaviorally oriented programs of the Alcohol, Drug Abuse, and Mental Health Administration.

Questions for Dr. Wyngaarden
from Senator Eagleton

(This question is answered in the transcript, pages 22-23; additional information is also provided for the record)

Question: S. 773 includes language designed to assure that the programs and activity levels of the arthritis division will not be diminished by the transfer to a new, separate institute and directs the Secretary to transfer to the new institute the "personnel, assets, liabilities, contracts, property. . . " etc. associated with arthritis, musculoskeletal and skin diseases. What will be the impact of this provision both with respect to the new institute and the remaining divisions in the diabetes institute?

Answer: The impact on the parent institute would be extremely harmful, resulting in either a reduction in essential management functions or vital research activity. To understand the difficulties involved, it is important to realize that NIADDK now experiences economies of scale because administrative services are provided centrally at the Institute level. For example, one budget officer and two analysts now provide all financial management services to NIADDK's ten programs. If the Arthritis Division were removed from NIADDK and reconstituted as a new institute, however, it would not be possible for the parent institute to reduce its financial management staff and still provide adequate services to the seven remaining high-priority programs in the institute, such as diabetes, digestive and kidney diseases, and metabolic diseases like cystic fibrosis. Similar difficulties exist in other administrative areas such as grants and contracts management, program analysis, research planning, and personnel management. Thus, we estimate that NIADDK could realistically transfer only about $800,000 to the new institute--representing the salaries associated with 16 positions directly assigned to the Arthritis Division. To transfer any more resources, as would be required by S. 773, would reduce administrative and management support services in the parent institute below levels necessary to maintain minimal functions, or alternatively, would reduce research support by an estimated 20-25 grants. Essentially, the parent institute would be bearing the brunt of meeting the overhead costs of creating the new, duplicative administrative structure, while the new institute itself would have to absorb only about one third of these costs.

Questions for Dr. DeVita from Senator Hatch

Question:

The total budget of the NCI now approximates $1 billion, I understand that management of this extraordinary sum is challenging, but nonetheless essential. Could you tell us what has been done to prevent future cases of fraudulent research such as those we discussed at our investigation hearings in June of 1981? Would it still be possible for any scientist under investigation for fraudulent research or misuse of funds to continue to receive grant monies from NCI?

Answer:

In 1981 the National Institutes of Health (NIH) created the ALERT System as a means of better managing investigations related to fraudulent research or misuse of funds. The National Cancer Institute (NCI) participates in this system, as do all the NIH Institutes. When an investigation commences, all Institute directors, appropriate Institute program officials, and relevant offices are advised of the allegations and the procedure for the investigation. The computer used by the entire NIH is coded so that any new application from the individual under investigation is flagged, indicating the existence of an investigation. Ordinarily, study section members are not notified of an ongoing investigation, although they are notified of any findings that result from the investigation, once it is completed, that are relevant to any scientific material under their review.

It is possible that an individual who is being investigated could receive grant funds. However, the NCI can decide to delay or cancel a technical review or delay or deny funding, with the concurence of the NIH Associate Director for Extramural Actvities, if we believe that there is just cause to do so. We would make these decisions on a case by case basis.

"Sections 401 and 403 were amended to require research be conducted related to continuing care of the cancer patient and the family of the cancer patient. This addresses the concern that a number of cancer victims suffer tremendous psychological, economic and social problems related to their illness." (page 14, Report No. 97-461)

The National Cancer Institute (NCI) agrees that this is an important and often overlooked area of research, therefore last year the NCI hired two individuals with specialized experience in the area of continuing care.

In May, 1982 the Institute hired Dr. Jerome Yates who was serving at the time as the Associate Director for Cancer Control of the Vermont Regional Cancer Center. Dr. Yates has extensive experience in the areas of costs related to cancer care, pain control, education of community nurses and physicians who care for cancer patients, and general outreach activities. We are in the process of evaluating the impact of the NCI's previous continuing care research efforts, and we anticipate new initiatives being developed in the areas of economic impact of cancer, psychosocial support systems for the patient and the family, pain management, quality of life issues and physical rehabilitation. Dr. Yates also has participated in the Advisory Committee of the National Hospice Study and we will be reviewing this material as it relates to the research program at the National Cancer Institute.

Dr. Lee Gigliotti has been hired as Chief of the Education Branch. Dr. Gigliotti is a nurse-educator who has been brought to the NCI to develop professional education activities with an emphasis on pain management and continuing care.

"The dollars devoted to cancer centers have increased over the past several years, but the proportion of the total budget devoted to cancer center support has gradually fallen. The Committee urges the NCI leadership to review this trend and maintain support for cancer centers at a level which will ensure their stability." (page 14, Report No.97-461)

The National Cancer Institute (NCI) has reviewed the allocation of the NCI budget dollars to cancer centers and has demonstrated that the proportion of NCI budget dollars devoted to core grants for centers has risen steadily since 1977. Actually, centers have received a greater portion of the total NCI budget virtually every year since 1977. Moreover, the dollars allocated to centers have increased even though the total NCI budget decreased in 1981 and 1982.

The Institute believes that cancer centers are essential to the progress we are making in cancer prevention, research and treatment. We have said on numerous occasions that the NCI is committed to this program, and we will do our absolute best to see that they receive the resources they need to continue their important work.

"The legislative authority for the National Cancer Advisory Board was left intact. Nonetheless, the Committee is concerned that individuals considered to fill vacancies should include those knowledgeable in environmental carcinogenesis." (page 15, Report No. 97-461)

Ten of the 18-member National Cancer Advisory Board (NCAB) have indicated an interest in environmental carcinogenesis. Of these 10, five are individuals that have scientific expertise in the area.

It may be worth noting that appointments to the NCAB are made by the President, who receives nominations from a variety of sectors of the Government, including the National Cancer Institute, and the private sector.

"The National Cancer Advisory Board has made approximately eleven reviews of the Organ Site Program over the last decade, all of which have supported continuation of organ site programming.... The Committee expects continued funding for these important programs and establishment of the recommended new task forces, as resources permit." (page 15, Report No: 97-461)

The Committee is correct in its citation of the numerous reviews that have been done of the Organ Site Program. The most important of these reviews is the one commissioned by the National Cancer Advisory Board (NCAB) in the fall of 1981. For the first time an independent body of scientists reviewed the program. These scientists noted several areas that needed restructuring, most notably the need to separate review from program. Early in 1982 the NCAB Subcommittee on the Organ Site Program, after discussing the results of the independent review, developed a set of recommendations for change that were passed unanimously by the full NCAB at its May 1982 meeting. Major components of these recommendations included the separation of review and program by bringing the review function into the normal NIH/NCI review system--including the establishment of special study sections as needed, establishment of one external coordinating center, continued emphasis on the genitourniary/gastrointestinal systems, use of existing NCI mechanisms for clinical trials research, and renaming of the program as the Organ Systems Program.

During the fall of 1982 the Organ Systems Subcommittee of the NCAB expressed an interest in reviewing the NCI implementation plans of the NCAB May recommendations, with a view to elaborating upon these recommendations. With the exception of the establishment of a single coordinating center, the Board's recommendations had been implemented. Accordingly, the NCI agreed to delay the issuance of the Request for Application (RFA) for the external headquarter's offices until such time as the Subcommittee could reconsider its recommendations. The funding of the existing four Organ Site Program headquarters was extended.

In late January 1983 the Organ Systems Subcommittee met for one and one-half days to review the restructuring of the Organ Site Program. With some modifications, the Subcommittee developed a set of recommendations consistent with the May 1982 NCAB recommendations, and after consideration and further modification, the full NCAB unanimously adopted the Subcommittee's organ systems recommendations.

The RFA establishing the external coordinating headquarters was issued in March 1983. An award is anticipated at the end of FY 1983.

The NCI has no plans to dismantle research related to specific organ sites; rather the Institute is restructuring and modernizing the program in order to increase its flexibility in dealing with areas that may need more attention and to make it more cost effective. It is thought that by following the recommendations of the NCAB, the deficiencies in the current administrative structure can be rectified and that organ site research will compete with all other significant research that is supported by the Institute.

"The Committee expects the NCI will continue funding cancer education programs. However, the Committee is concerned whether NCI should continue to fund a large number of post-doctoral training programs in oncology when the need for these specialists is likely to decline in view of the Graduate Medical Education National Advisory Council (GMENAC) report projections of imminent physician surplus." (page 16, Report No. 97-461)

Only a few years ago a cadre of cancer specialists did not exist in this country. National Cancer Institute (NCI) training programs in research and clinical medicine have seeded the country with cancer specialists. The Institute agrees that it is important to coordinate our training efforts with national trends and we are doing so. About a year ago we revised our training guidelines and established the Professional Oncology Training Program. This program is not limited to medical and dental schools and their affiliated hospitals. Rather, training opportunities are available for all health professionals, including undergraduate students. The goal of this program is to integrate the teaching of cancer epidemiology, prevention, nutrition, and cancer control with clinical and basic science in the management of cancer.

Of the 154 NRSA individual fellowships awarded by the NCI in FY 1982, only seven were awarded to physicians.

Questions for Dr. Lenfant
from Senator Hatch

Q. Could you briefly cite for us the most promising areas of research in NHLBI with respect to what remains our number one killer - heart disease?

A. Over the past two years the Institute and its Division of Heart and Vascular Diseases have conducted a review of progress in heart disease by 11 scientific Task Groups. Recommendations of the most promising area for further research over the next five years have been provided, and will be of value in the selection of areas for emphasis over the period through 1987.

Promising areas for research relating to five of the major heart disease problems are as follows:

In Arteriosclerosis promising findings can be expected in:

- Understanding of the basic pathogenetic mechanisms of atherosclerosis at the tissue, cellular, and molecular levels using new techniques, including those of cellular and molecular biology;
- Knowledge of the causal mechanisms and associated risk factors that play important roles in atherogenesis;
- Understanding of the natural history of arteriosclerosis in such vascular regions as arteries of the heart, brain and legs in humans, by utilizing modern methods of research;
- Better understanding of the epidemiology of arteriosclerotic disease, by improving data gathering capability and analytic methods, and thus improving our ability to predict arteriosclerosis in our populations;
- Developing minimally invasive and noninvasive methods for detection of atherosclerosis in various regions of the vascular system;
- Investigations to determine the effectiveness of therapeutic interventions to reduce or prevent atherosclerosis, and to learn more about the roles of behavior in the causation and prevention of arteriosclerosis; and
- Characterization of risk factor distributions and their changes over time, and better understanding of health-related behaviors especially in youth, and fostering healthful habits.

In Hypertension much progress has been made in its treatment, but there is need to increase our basic knowledge of the causes of this disease. Particular areas for research progress are in:

- Fundamental interdisciplinary research on the etiology and pathogenesis of hypertension, including investigations in neural, humoral, genetic and environmental factors;

- Investigation of the influence of familial, genetic and environmental factors in the determination of blood pressure levels of all age groups, to establish their relative importance in contributing to the development of high blood pressure:

- Development and refinement of noninvasive techniques for measurement of blood pressure, heart size and biochemical tests related to hypertension to be used for the evaluation of the health status of persons with high blood pressure;

- Improvement of pharmacologic and nonpharmacologic methods for the long-term management of hypertension and evaluation of their relative roles in terms of benefits as well as risk. Continuing the study of the benefits and risks of blood pressure reduction in elderly individuals with systolic hypertension;

- Improved control of high blood pressure in the population, (especially in segments of the population where the disease is prevalent) through demonstration and education activities; and

- Continuation of research and development programs that attract and sustain high caliber hypertension research investigators who will maintain progress against this disease.

In Coronary Heart Disease more effective treatments continue to be developed and are improving the survival of patients who suffer an acute heart attack. Promising further areas for research in coronary heart disease are presently being directed to:

- Better understanding of the fundamental pathogenetic mechanisms involved in coronary heart disease and its various manifestations, including sudden death;

- Development and refinement of methods for diagnosing and estimating prognosis in patients with asymptomatic and symptomatic coronary heart disease;

- Refining improved medical and surgical procedures for the treatment of acute coronary events and chronic ischemic heart disease;

- Identifying factors involved in the pathophysiology of coronary heart disease and the transition from asymptomatic to clinically symptomatic disease;

- More effective rehabilitation of patients with coronary heart disease;

- Enhancing methods to reduce or prevent new and recurrent myocardial infarction; and

- In subpopulations identified as being at especially high risk for coronary heart disease, improving the detection of such individuals and developing methods to modify their risk factors including health-related behaviors.

In Arrhythmias of the heart which can be life threatening there are increasingly effective methods for management with drugs and with implantable pacemakers. Further promising areas of research are in:

- Identification of the fundamental electrophysiologic mechanisms of normal and ischemic heart muscle and their relationship to sudden death;
- Development and refinement of methods useful in identifying individuals in all age groups who are at risk of sudden death;
- Improving the understanding of the nervous system and its role in the pathogenesis of cardiac rhythm abnormalities; and
- Developing and refining medical and surgical treatments to reduce or prevent sudden death in high risk populations.

In Heart Failure and Shock which are the most serious stages of heart disease there have been important advances in the ability to measure failing heart function and apply new drugs which act to strengthen the heart's function. Temporary ventricular assist devices and progress toward permanent artificial heart devices are continuing areas of research. Further research opportunities are seen in:

- Better the understanding of the basic mechanisms and the natural history of heart failure and shock;
- More effective techniques for the clinical detection, treatment, and prevention of heart failure and shock;
- Improving techniques of cardiac transplantation and immunotherapy which offer another therapeutic approach in certain patients whose heart failure is refractory to all other measures;
- Development and improvement of short-term ventricular assist devices which can support the circulation during the period needed for recovery of the function of the failing heart; and
- Continuing to develop effective, safe and reliable total cardiac replacement devices for selective use in humans.

Q. Last year we applauded your institute for efforts in behavioral medicine recognizing a significant factor in most diseases, and particularly heart disease, as related to lifestyle and stress. However, we also conveyed concern that this effort was likely inadequate given the limited number of staff and resources devoted to this. What has been done in the intervening time to increase your research in behavioral medicine?

A. NHLBI funding for biobehavioral research increased from $14.8 million in FY 81 to $20.4 million in FY 82. Corresponding figures for the Behavioral Medicine Branch are $7.33 million and $9.52 million, or just under 50% of the total biobehavioral research expenditures for the Institute.

In addition to investigator-initiated research program applications, proposals were received in response to two Program Announcements (Biobehavioral Approaches to the Treatment of Hypertension; Psychosocial Mediators for the Maintenance of Smoking Cessation) and one Request for Applications (Genetic and Developmental Factors in the Etiology and Progression of Hypertension).

Institutional biobehavioral research training awards (NRSA) have been steadily increasing over the past five years, with eleven programs currently funded. One, possibly two, additional training programs may be funded in FY 83.

During the past year:

- A program initiative (RFA: Biobehavioral Factors Affecting Hypertension in Blacks) and the working conference on CHD in Blacks were approved for funding.
- A working conference entitled "Cardiovascular Instrumentation: Applicability of New Technology to Biobehavioral Research" was held in Houston, Texas, co-sponsored by Baylor College of Medicine.
- Two working groups were formed:
  1) Biobehavioral Treatment of Hypertension
  2) Experimental Design and Research Methodology in Cardiovascular Behavioral Medicine.
- Proceedings for the conference on "Circulation, Neurobiology and Behavior" (co-sponsored by the University of Texas Health Sciences Center - Dallas) were published by Elsevier.

In terms of program areas, coronary heart disease and hypertension are the primary focus for perhaps 85% of Behavioral Medicine Branch grants, with the majority concerned with coronary heart disease. Examples of recent research developments include a new animal model for hypertension which exemplifies the biobehavioral approach to the development of disease. It has been developed through studies of the effects of a combination of avoidance conditioning and saline infusion upon cardiovascular adaptations of chronically instrumented dogs. In this animal model, only modest elevations in blood pressure were observed when either avoidance conditioning (a behavioral stressor) or salt loading (a physiological stressor) was used alone. However, a combination of these stressors dramatically increased blood pressure (3 of 6 dogs experienced cerebral hemmorhages within 3 weeks) suggesting that the interaction of behavioral and physiological variables has a synergistic effect on blood pressure elevation.

Efforts to explain how lifestyle, stress, and behavior influence the development of disease have led to increased biobehavioral research on the basic mechanisms of cardiovascular and neuroendocrine responses to stressors. Several NHLBI-supported research projects are currently investigating individual differences or hemodynamic reactivity over time, and in reactions to various natural stressors or laboratory manipulated conditions. Subjects categorized as exhibiting a coronary-prone behavior pattern (Type A) showed significantly greater cardiovascular changes indicative of sympathetic autonomic nervous system arousal when presented with a challenging task as a stressor than did subjects identified as Type B. Current research suggests that inappropriate, prolonged, or exaggerated physiological responses of such individuals to environmental and emotional stressors may contribute to the observed increased disease risk among persons identified as having coronary prone behavior patterns.

Coronary prone behavior patterns and related physiological reactivity have also been investigated in pediatric groups. Researchers report that Type A (coronary prone) behavior can be measured in children and tracked over time in a large (n=600) pediatric sample. Like Type A adults, Type A children were found to suppress fatigue during a strenuous task, show heightened blood pressure and heart rate responses to a psychological challenge, and make active efforts to exert control over stressful conditions.

In a recent study on secondary prevention, 900 post myocardial infarction patients were randomized into 3 groups, a) cardiology counseling, b) Type A behavior change plus cardiology counseling, and c) usual care. After four years of treatment, significant reductions in mortality were observed in the "Type A behavior change plus cardiology counseling" group as compared with the other two groups. It appears that behavior change counseling to decrease Type A behavior exerts an effect on mortality beyond that produced by cardiology counseling alone.

Progress in staffing the program has been encouraging, with all seven slots filled at this time. Given personnel limitations for the Institute, only three (one scientific, two administrative) positions currently are permanent. Over the next year, efforts will be undertaken to enhance program continuity through increasing the number of permanent staff positions in this program.

Question for Dr. Salans
from Senator Hatch

Question: I have recently met with directors of the advisory boards for diabetes, arthritis and digestive diseases. They all cited concerns about inadequate funding for their research effort. Could you tell the Committee how the budget for these three areas of research is allocated?

Answer: I am pleased to comment on the budget process of the National Institute of Arthritis, Diabetes, and Digestive and Kidney Diseases (NIADDK). Our first consideration in allocating resources is to respond to Congressional directives and intent as reflected in legislation, report language, and communications with the Congress. Our second consideration is to meet existing commitments for grants and contracts which were awarded in previous years. Once these two priorities are met, we begin to develop operating plans for allocating the remaining funds available to us in any given fiscal year.

I am very pleased to report that, with elevation to bureau status and changes in leadership, NIADDK has initiated a new budget process. The driving force of this process is the identification of scientific opportunities, gaps, and needs, with consideration of the concerns of the public as expressed through Congress, the Executive Branch, advisory groups and national advisory boards, and health voluntary and professional organizations.

An important factor in this process is the availability of a critical mass of basic knowledge with which to launch scientific inquiries. We therefore rely heavily on the scientific community to identify, through the peer review process, the most meritorious scientific ideas and the investigators most able to respond to policies and priorities shaped by Congress and the public, and therefore most worthy of support.

Through the competitive research grant system, we are able to tap the best ideas, which are weighed by scientific peers for scientific merit and methodology. Proposals are further evaluated by the Institute's National Advisory Council for program relevance, a process which enables us to identify for funding areas of special need or emphasis.

Central to our new planning and budgeting process are greater involvement of the entire research community, increased budget flexibility for each NIADDK division, and an effort to ensure a fair and equitable allocation of resources. Continuous monitoring and necessary adjustments throughout the year in response to changing scientific opportunities and needs.

We believe this new approach is quite successful and are submitting for the record a summary of the Institute's new budgeting process.

NIADDK Budget Allocation Method

The Institute is required to support a specific number of new and competing research projects and NRSA research trainees each fiscal year. In addition, the NIADDK occasionally receives Congressional mandates (earmarks) to support specific research activities. The Institute will first utilize any increases in appropriated funds to satisfy these requirements. Remaining funds will be available to support Extramural research through other mechanisms - Centers, Research Career Awards, Contracts - and to conduct Intramural research.

The primary emphasis of the budget process is budgeting according to Divisions. This permits each Associate Director a much greater degree of flexiblity for budgeting among individual Programs within a Division than previously existed. Initial allocation of increases or decreases of funds appropriated to the Institute for a given fiscal year is based on an agreed upon set of guiding principles, and distributed to the Division according to the best projections available at the begining of the fiscal year. As the year progresses, the impact of the initial allocations on each Division will be examined and adjustments made to ensure that they follow the guiding principles and criteria. It is important to recognize that Division and Program budget projections made at the beginning of a fiscal year, or two years in advance, are estimates only and are not fixed in concrete at those times, and final budgets will only be available at the end of the fiscal year.

The guiding principles and criteria include:

1. Priority score paylines - Discrepancies in paylines between Divisions and Programs will not be greater than a certain number of points. Please note that there is a considerable variation of priority scores between Study Sections. The mean priority score of two separate Study Sections, both feeding grants into NIADDK Programs has differed by as much as 50 points. Thus, a grant score of 200 received from two different Study Sections may not indicate equal scientific merit. The Institute is studying this question and the data will be made available to you. Clearly, the magnitude of the difference in paylines between Divisions and Programs that will be allowed will be influenced by this factor. If priority scores are to be a meaningful criteria, this question must be dealt with each year.

2. Award rates - Variation in the percentage of approved grants that are funded between Divisions and Programs will be minimized and, where possible, kept at a level between, for example, 5% and 10%. Generally, priority scores and award rates follow each other, but occasionally this is not the case. In such instances, both the priority score payline and the award rate will be taken into consideration.

3. Other mechanisms - Mechanisms other than Research Project Grants and Research Training, i.e., Research Centers, Research Career Awards, and Contracts are also used to support research.

4. Special opportunities or needs - The allocation of funds determined according to principles 1) and 2) is subject to modification if special and unique opportunities and needs present themselves in specific programs.

5. Other modifying factors - Other factors are also applied, such as the total budget of each Division, rate of growth of Division budgets, the state of the science in each area, the magnitude of the public health problem, and Congressional and Administration directives.

6. Small reserve - A small amount of each Division's budget is held in reserve for each Council (three per year). This resource is used by the Director, to selectively supplement Program budgets in order to ensure conformity with the guidelines described above.

Question: We have received a significant number of requests to encourage you to provide funds to investigate mycoplasma as the cause of rheumatoid arthritis. These requests come from various sincere individuals who have received treatment from physicians whose methods are apparently not widely accepted. What is your opinion about this request?

Answer: The Institute believes that it is currently funding the very best research and researchers in the area of arthritis. Research applications and proposals submitted by investigators in the field to the Institute are reviewed through a two-step, rigorous peer review process through which the most meritorious and highly promising research ideas are identified for funding within the limits of resource availability.

In Fiscal Year 1982, the National Institute of Arthritis, Diabetes, and Digestive and Kidney Diseases (NIADDK) expended approximately $300,000 on research related to mycoplasmas and arthritis. This included funding for one career development award, one research project in a multipurpose arthritis center, and four regular research grants. These projects are just one part of the Institute's broad research effort aimed at improving our understanding of and treatment for arthritis.

Evidence from research, including that supported and conducted by NIADDK, indicates that a complex series of factors is involved in the development of rheumatoid arthritis. Major areas of research include studies of immune defects, which may result in the chronic inflammation of the disorder; research on a whole host of infectious agents, including viruses and bacteria, as well as mycoplasmas; and studies on genetic markers for rheumatoid arthritis, which may help identify persons most susceptible to the disorder. Other areas of research on the causes of rheumatoid arthritis include the possible roles of hormones, metals and other substances.

With NIADDK support, numerous researchers are also searching for more effective treatments for rheumatoid arthritis. Examples of experimental therapies that show promise include: immunosuppressive drugs such as methotrexate; modified forms of corticosteroids, which may have the benefits of corticosteroids with fewer risks; and a new form of gold taken orally rather than by injection. Other possible therapies are a blood filtering technique known as apheresis, which may remove substances that cause chronic inflammation and joint damage, and irradiation of the lymph tissues to suppress the immune system and induce a remission of the disorder.

We believe that these comprehensive research efforts, which reflect investigator-initiated research judged most meritorious by the competitive NIH peer review process, remain the most promising and productive approach to combatting rheumatoid arthritis and other forms of arthritis.

Questions for Dr. Cummings
from Senator Hatch

(These questions are answered in the transcript, pages 31-33 and 34-35).

Question from Senator Dodd

Q: What should be the role of the Congress in protecting the interest and investment of taxpayers whose tax dollars support much of the Nation's research effort?

What should be the proper role of private industry in funding applied R&D?

Should the legislation on the current patent laws be amended to assist individual researchers in commercializing products that result from research?

A: Any national policy seeking to maximize the public interest in this area must assure that adequate financial incentives exist for the practical exploitation of biomedical knowledge on behalf of the public health. Public Law 96-517 established this principle by providing to non-profit organizations and small businesses the first option to ownership of all inventions they make in the performance of federally funded research. DHHS has followed the policies in the new Patent Act since the mid-1960s, and our experience has been very positive. In the event that a private sector licensee is not developing a product needed for the public health, the government can step in. Appropriate financial incentives for private sector licensees, plus these potentially coercive rights of government, have served to promote the practical development of drugs and devices in the interest of the public health. While the new genetic engineering has attracted a good deal of public attention, and is serving to reshape to some extent relationships between universities and business firms, this field has not yet raised issues of such concern as to shift the fundamental balance between public and private sector funding of new health innovations. For this reason, it is the view of the Administration, in light of the positive findings under P.L. 96-517, that its policies be extended to all other federally funded contractors. This has been done, to the extent provided by law, by a February 18, 1983 Presidential Memorandum. The Administration would view favorably a legislative initiative to eliminate conflicting legislation.

The historic role of private industry has been to fund applied R&D in the development of new drugs and devices. In some areas, e.g., cancer drugs, orphan drugs, and comparative clinical trials of different therapies, government agencies (particularly the National Institutes of Health and the Veterans Administration) have also contributed to R&D funding. This general balance of roles is continuing to occur in the commercialization of products growing out of the new biotechnology. The bulk of the applied work in development, e.g., interferon, DNA-derived insulin and growth hormone, and other emerging therapies, is being supported by the private sector. Basic biomedical research on which these innovations rest, however, is largely a public sector contribution.

Questions for Dr. Brandt
from Senator Dodd

Several bills were introduced in the 97th Congress to examine research methodology, upgrade animal care institutional standards, and revise or expand present institutional animal care committees. I support many of these efforts. Many opponents of the use of animals in research, however, advocate that there are sufficient alternative methods which preclude the need for animals in research.

Are there such alternative methods in existence? How effective are these alternative methods?

Half of all the research efforts supported by the NIH use "alternatives" since no live animals are used in the conduct of the research and all of the research either directly or indirectly increases our understanding of human biology in disease and in health.

Animals are used in research when the research questions asked warrant such use. When research questions undergo modification, situations may arise in which a problem originally studied using a mammalian model can now be examined at a different level in tissues or cells in culture or in some other simple model system. There may be occasions when there is a scientific value in moving from one "model system" to "another", where one system is a complex living organism, and the other a less complex simple system such as cells or tissues in culture. The mechanistic aspects of a disease, discovered and identified in a mammalian model, may best be studied using cells in culture. The results from the cell culture studies may in turn lead to the development of a drug, the efficacy of which must be determined using the original mammalian model.

The Division of Research Resources, at the NIH, through its Biomedical Research Models Development Program, is trying to determine the general applicability of the simpler model systems now in use in biomedical research. The Division is particularly interested in determining the general applicability of model systems using terminally differentiated human cells, select invertebrate systems and mathematical/computer simulations to major biomedical research problems.

What would be the extent of increased institutional costs in adhering to the standards proposed by these legislative efforts?

Bills introduced in the 97th congress would have required that animal facilities at research institutions receiving Federal funds for research or testing involving the use of animals be accredited by a primate agency or through a government mechanism. This accreditation would have entailed certification of an initial achievement of high standards, as defined both by the legislation and by the accrediting body, and regular recertification that those standards were being maintained. Currently, accreditation of animal facilities by the American Association for Accreditation of Laboratory Animal Care (AAALAC) is based on compliance with guidelines set forth in the National Institutes of Health (NIH) "Guide for the Care and Use of Laboratory Animals." These guidelines were also reflected in the proposed legislation.

At hearings before the House Subcommittee on Science, Research, and Technology in May 1982, an estimate was provided of the cost to research institutions to comply with the "Guide." This estimate was based on information contained in a survey completed in 1978 by the Institute of Laboratory Animal Resources (ILAR) of the National Academy of Sciences National Research Council. The executive summary of this survey ("National Survey of Laboratory Animal Facilities and Resources") includes the statement that $350 million [is estimated to be needed] to meet current needs of nonprofit biomedical research organizations for space replacement, remodeling, and additions . . . another $407 million . . . will be required to meet space needs projected for

FY 1988." The estimate of $500 million provided to the House Subcommittee was an extrapolation based on 1982 construction costs.

According to the ILAR survey, approximately 10 million net square feet of laboratory animal facilities was being used at research institutions eligible to receive NIH research funds. About 38 percent of this space was reported to need remodeling and another 16 percent to need replacement. This did not include renovations or other alterations that would be done in the course of routine maintenance. As of this date, very little of that work has been done. Therefore, costs for remodeling and replacement of about 3.8 million and 1.6 million square feet respectively are still relevant today.

The ILAR survey also reported that the numbers of animals purchased or bred for research purposes had declined somewhat over the last 10-15 years. However, this does not mean that less space is needed. On the contrary, one important reason for declining animal acquisition is that more long-term and chronic studies are being done, for which animals are maintained for long periods of time. This does not lead to reduced need for animal facilities.

Question:

There has been increased support for the legalization of heroin for terminally ill cancer patients. What benefits would heroin provide terminally ill patients that are now unavailable in drugs currently being used for these individuals?

Are there drugs, other than heroin, which are not legalized for the treatment of terminally ill patients which could offer substantial benefits?

Answer:

Numerous studies indicate that heroin does not provide a unique contribution to the treatment of pain in cancer patients. Drugs are currently available that are powerful enough to treat severe and long-term pain. Dilaudid (hydromorphone) is an excellent example of a morphine analog that is nearly twice as potent as heroin, peaks earlier than heroin, and has a longer duration than heroin. Problems in pain management result not only from a lack of understanding about the availability of narcotic drugs but appear to have arisen because of fears physicians and other health professionals have about addiction and overdose.

Because heroin does have a solubility advantage in muscle-wasted patients who are tolerant to the usual doses of narcotics, the Food and Drug Administration (FDA) has sought and obtained commitments from two drug firms to reformulate already available narcotic analgesics into more concentrated dosage forms suitable for such patients. We expect that the firms will complete their current studies and file New Drug Applications (NDAs) with FDA in 1983.

The National Cancer Institute (NCI) is not aware of any drugs that are not legalized that would be useful for the treatment of pain in cancer patients.

Questions for Dr. Cummings

from Senator Dodd

QUESTION: Are the current reimbursement methods for services rendered by NLM sufficient to cover costs of providing these services?

ANSWER: The National Library of Medicine currently recovers the full cost to access its online retrieval system and recovers the full cost, through licensing arrangements, for MEDLARS computer tapes leased to foreign and domestic vendors. The current pricing policies for NLM have been reviewed by the GAO and OTA and they have essentially concluded that NLM policies are consistent with statutes and regulations.

QUESTION: Should the services of NLM be restricted to specific individuals and institutions?

ANSWER: Under the National Library of Medicine Act, NLM services are available to the entire medical and public health communities. Therefore there should not be any restrictions which would deprive health professional users from access to Library materials or services.

The CHAIRMAN. Our second panel consists of a distinguished group of scientists who are going to provide testimony regarding the recent accomplishment of NIH-funded research. Our first witness will be Dr. Timothy Talbot, chairman of the board of the Association of the American Cancer Institutes. Dr. Talbot recently retired as president of the Fox-Chase Cancer Center in Philadelphia, one of the leading centers for cancer research and treatment in the country. The second witness is Dr. Samuel Fox III. Dr. Fox is a distinguished faculty member at the Georgetown University College of Medicine and past president of the American College of Cardiology. I am also very pleased to welcome our third witness on this science panel, Dr. John Dixon, who is one of my constituents, a professor of surgery at the University of Utah College of Medicine. Dr. Dixon will provide testimony regarding research in digestive diseases conducted by NIADDK, and I understand Dr. Dixon is the only Utah physician, as I mentioned before, who has served as both the dean of the University of Utah College of Medicine and the president of the Utah State Medical Association. Our fourth witness in the science area will be Dr. Ephraim Engleman, a distinguished specialist in rheumatology at the University of California at San Francisco. Dr. Engleman is representing the Arthritis Foundation.

We are very happy to have you gentlemen with us. Dr. Talbot, would you begin, please.

STATEMENT OF DR. TIMOTHY R. TALBOT, JR., CHAIRMAN OF THE BOARD, ASSOCIATION OF AMERICAN CANCER INSTITUTES

Dr. TALBOT. It is a privilege for me, Mr. Chairman, to be here on behalf of the Association of American Cancer Institutes, which we call the AACI. I am Dr. Timothy R. Talbot, Jr. I am now chairman of the board of the AACI and former president of the Fox Chase Cancer Center in Philadelphia, where for 25 years or a little more I have been engaged in developing a major cancer center. This has been a rewarding and exciting experience and undertaking for me, as you can imagine, especially in view of the remarkable explosion in knowledge that is now beginning to come into full flower in the entire biological and biomedical arena. This includes, as you are fully aware, remarkable promising potentials in the clinical and fundamental sciences relating to cancer.

Today, I want to focus briefly on three important points: the philosophy and purposes that have led to the development of cancer centers in the Nation, some research accomplishments and capabilities of the cancer centers as brief examples, the importance of maintaining a stable base of support for the cancer centers, especially in view of their prominent role in the fundamental and clinical aspects of biomedical science as these are related to cancer.

There were already several competent cancer centers in existence when the National Cancer Act was passed by the Congress in 1971. As I understand it, the National Cancer Institute already had at that time all of the authority that it needed to support the programs of these and other centers. The only rational conclusion that one can draw from the passage of the act, therefore, and the authorities for the cancer centers within it, is that the Congress wished to give special emphasis to the cancer problem. As it did so, it also gave prominent emphasis to the value of cancer centers, both present and future. These centers were expected to and have become important reservoirs of competence in basic biomedical research related to cancer, and to become equally important resources for conducting clinical investigation of high quality.

Many cancer centers receive grants, called core grants, from the NCI to pay for research resources which can be shared by investigators whose individual research grants would not otherwise cover the full cost of their work. These core grants provide central support services and highly specialized laboratory services that are uniquely suited to the common interests of several investigators working in close proximity in a coordinated fashion within these centers.

All of this, fortunately was to be done within the framework of the peer review process. The major emphasis and thrust of centers was clearly aimed at gaining important new knowledge—in other words, doing high quality scientific research in both the laboratory and clinical arenas. It should also be emphasized that the large number of RO-1 and PO-1 grants that have been awarded to centers have been based on a stringent peer review system for which we are all grateful, which is a valid measure of creative excellence. I shall not try to burden you or the committee with excessive amounts of information but would like to give quickly some examples of the kinds of advances that have been brought about by research in these centers.

As one example, at the Fox Chase Cancer Center, the work on Dr. Baruch Blumberg on hepatitis B virus, work for which he won the Nobel Prize, and primary cancer of the liver which is associated with that virus demonstrate how a cancer center program facilitates the transition of basic research to clinical care. There is a group of people who are at high risk of developing primary cancer of the liver because of a high rate of persistent infection with hepatitis B virus. We are now in the process of applying the findings of this work to the control of this primary cancer. This requires the utilization of our clinical facilities and our cancer control and education staff. This is one of the first instances where a major cancer may be controlled by prevention and/or early detection and treatment and, as noted, the work has been done in a cancer center utilizing the findings of basic science and transferring them quickly through basic research. Thus we have a vaccine against hepatitis, which in all likelihood will prevent the most common cancer in the world or one of the two most common cancers if public health measures can be adequately pursued.

In another example, bone marrow transplantation units for the control and treatment of acute lymphocytic leukemia and related diseases were first developed in cancer centers in Seattle and Baltimore. These units require enormous backup of clinical and basic reseach, both on the nature of the disease and the immunologic implications of the treatment. This treatment is now available in cancer centers in Boston, New York, Houston, Memphis, and Philadelphia, as well as in Seattle and Baltimore.

Finally, I cannot let this opportunity pass without referring to an application of the revolution that has occurred in modern biology to the cancer problem. The use of monoclonal antibodies for diagnostic and therapeutic purposes in cancer is a process which requires close cooperation between the basic sciences and the clinicians. Development of these techniques is currently underway in a number of cancer centers throughout the country and probably can only be done in the type of environment these centers offer.

We are witnessing, as this committee has heard from many respected sources, an explosion of important, exciting, and apparently increasingly relevant new scientific information. These advances are being provided by the entire biomedical research community of the Nation and perhaps the world, but it is our belief that the potentialities for further advances in the immediate and long-range time frames will be greatest for the cancer field in the laboratories and clinics of these centers.

What we are now watching is undoubtedly due to the relative stability of support for biomedical research and centers that the Congress, including this committee, has provided during the last three or four decades. The single most important aspect of support for these endeavors is clearly a rational stability. The rewards of past support and effort are now coming in. We must see to it that our efforts in this decade will continue so that we will always have an ongoing developing reservoir to help us deal with the future. For these reasons, we, among many of our colleagues, continue to plead the case for stable funding at the cancer centers and the entire biomedical research system of the Nation.

Mr. Chairman, we also wish to express our thanks for the recognition of cancer centers that was given by this committee in bill report language last year.

We also wish to call attention to the excellent testimony that you have already heard from Dr. Frank Rusher, who is now with the American Cancer Society and was formerly another of the highly respected directors of the National Cancer Institute, and we find ourselves in agreement with that testimony of his.

Finally, Mr. Chairman, we wish to express our thanks for the extraordinarily cooperative efforts and work of the various members of the staff of this committee. This includes especially Dr. David Sundwall and many others. They have made it possible for us to conduct a reasonable and very useful dialog. We also wish to place ourselves at your disposal if we can be of any help in any way in the future in providing future information or any evaluations that may be of help.

The CHAIRMAN. Thank you, Dr. Talbot. I have not been over to your hospital but I would like to do that. I went to M. D. Anderson a couple of years ago, and it was a great experience for me.

Dr. TALBOT. We would enjoy having you, sir. We did have several members of the staff visit us, among them Dr. Sundwall, and I think we both had an enjoyable time. They all asked questions that probed and prodded us, and I think we had fun showing them what this kind of operation can be like.

[The prepared statement of Dr. Talbot follows:]

PREPARED STATEMENT OF TIMOTHY R. TALBOT, JR.

Thank you, Mr. Chairman. It is a privilege for me to be here on behalf of the Association of American Cancer Institutes (AACI).

I am Dr. Timothy R. Talbot, Jr., Chairman of the Board of AACI, and former President of the Fox Chase Cancer Center in Philadelphia, where for 25 years I have been engaged in developing a major cancer center. This has been a rewarding and exciting undertaking and experience, especially in view of the remarkable explosion in knowledge that is now beginning to come into full flower in the entire biological and biomedical arena. This includes, as you are aware, remarkably promising potentials in the clinical and fundamental sciences relating to cancer.

The Association of American Cancer Institutes had its origin in 1958 and now has about 70 institutional members, including all of the centers that are recognized by the National Cancer Institute as being Comprehensive Cancer Centers. It is our common purpose to do all that we can to maintain a continuing momentum and forward thrust in our national effort in the attack on the problem of cancer.

Today, I want to focus briefly on three important points:

- The philosophy and purposes that have led to the development of cancer centers in the nation.
- Some research accomplishments and capabilities of the cancer centers.
- The importance of maintaining a stable base of support for the cancer centers, especially in view of their prominent role in the fundamental and clinical aspects of biomedical science as these are related to cancer.

Philosphy and Purposes

There were already several competent cancer centers in existence when the National Cancer Act was passed by the Congress in 1971. As I understand it, the National Cancer Institute already had, at that time, all of the authority it needed to support the programs of these and other centers. The only rational conclusion one can draw from the passage of the new law, and the authorities for cancer centers is, therefore, that the Congress wished to give special emphasis to the cancer problem; and as it did so, it also gave prominent emphasis to the value of cancer centers - both present and future. These centers were expected to become important reservoirs of competence in basic biomedical research related to cancer, and to develop equally important resources for conducting clinical investigation of high quality in a coordinated fashion.

Many cancer centers receive core grants from the NCI to pay for research resources which can be shared by investigators whose individual research grants would not otherwise cover the cost of their work. Cancer center core grants provide central support services and highly specialized laboratory services that are uniquely suited to the common interests of several investigators working in close proximity within a cancer center.

All of this was, fortunately, to be done within the framework of the peer review process. The major emphasis and thrust was clearly aimed at gaining important new understandings - in other words, doing high quality scientific research in both the laboratory and clinical arenas. It should also be emphasized that the large number of R-01 and P-01 grants that have been awarded to centers have been based on a stringent peer review process (for which we are all grateful), which is a valid measure of creative excellence. I shall not try to burden the committee with excessive amounts of information, but would like to give some examples of the kinds of advances brought about by research in these centers.

Research Advances in Centers

At the Fox Chase Cancer Center the work of Dr. Baruch S. Blumberg on Hepatitis B virus - work for which he won the Nobel Prize in 1976 - and primary cancer of the liver, demonstrates how a cancer center program facilitates the transition of basic research to clinical care. There is a group of people who are at high risk of developing primary liver cancer because of a high rate of persistent infection with Hepatitis B virus. We are now in the process of applying the findings from our laboratory and clinical research to the control of this primary cancer. This requires the utilization of our clinical facilities and our cancer control and education staff. This is one of the first instances where a major cancer may be controlled by prevention and/or early detection and treatment, and as noted, the work has been done in a cancer center utilizing the findings of basic science and transferring them quickly through clinical research to applied clinical activities.

Another example: bone marrow transplantation units for the control and treatment of acute lymphocytic leukemia and related diseases were first developed in cancer centers in Seattle and Baltimore. These units require enormous back-up of clinical and basic research both on the nature of the disease and the immunologic implications of the treatment. This treatment is now available in cancer centers in Boston, New York, Houston, Memphis, Philadelphia, as well as in Seattle and Baltimore.

Finally, I cannot let this opportunity pass without referring to an application of the revolution that has occurred in modern biology to the cancer problem. The use of monoclonal antibodies for diagnostic and therapeutic purposes in cancer is a process which requires close cooperation between the basic research laboratory and the clinician. Development of these techniques is currently under way in a number of cancer centers throughout the country and probably can only be done in the type of environment a cancer center offers.

We are witnessing, as this committee has heard from many respected sources, an explosion of important, exciting and apparently increasingly relevant new scientific information. These advances are being provided by the entire biomedical research community; but it is our belief that the potentialities for further advances in the immediate and long-range time frames will be greatest for the cancer field in the laboratories and clinics of the cancer centers.

Stability of Support

What we are now watching is undoubtedly due to the relative stability of support for biomedical research and for centers, that the Congress, including this committee, has provided during the last three or four decades. The single most important apect of support for these endeavors is, clearly, a rational stability. The rewards of past support and effort are now coming out - we must see to it that our efforts in this decade will be continued so that we will always have our on-going developing reservoir to help us deal with the future. For these reasons we, among many of our colleagues, continue to plead the case for stable funding of the cancer centers and the entire biomedical research system of this nation.

Mr. Chairman, we wish to express our thanks for the recognition of cancer centers that was given by this committee by bill report language last year.

Also, I want to be sure that you and the members of your committee are made fully aware of the intelligent and attentive communication that has been made possible by your professional staff members. This includes especially Dr. David Sundwall, Dr. Wes Clark, and many others who are here this morning. They have all made it possible for us to conduct a reasonable and useful dialogue.

We also wish to place ourselves at your disposal if we can be of help in any way, including the providing of information or evaluation whenever it can be useful.

Thank you for your attention and interest.

The CHAIRMAN. I would like to do that. I think I will take all the testimony and then ask questions a little later.

Dr. Fox, we turn to you at this point.

STATEMENT OF DR. SAMUEL M. FOX III, PROFESSOR OF MEDICINE, GEORGETOWN UNIVERSITY MEDICAL CENTER, ON BEHALF OF THE AMERICAN COLLEGE OF CARDIOLOGY

Dr. Fox. Thank you, Senator. I am Dr. Samuel M. Fox, professor of medicine at Georgetown University. I appear before you today representing the 12,000-member American College of Cardiology, of which I am a past president. We appreciate the opportunity to comment on various provisions of S. 773, the Biomedical Research Training and Medical Library Assistance Amendments of 1983, with particular relevance to the National Heart, Lung, and Blood Institute but also relevant to the National Library of Medicine.

It is the opinion of our organization that the performance of the National Heart, Lung, and Blood Institute has been exemplary under the current statutory authority, and it is highly probable that the Institute would continue to perform admirably if the authority were merely extended without amendment, provided sufficient funds were available to allow the Institute to address the many vital issues falling under its broad responsibility. We are particularly grateful to you for your recognition of this, as evidenced by your approach in S. 773.

The authorization of appropriations for each fiscal year is one issue for which we recommend amendment. As the responsibility of the NHLBI is broad, with 4 of the 10 leading causes of death and disability falling under its jurisdiction—namely, disease of the heart, which is the No. 1 cause of death and disability; cerebral vascular disease, No. 3; chronic obstructive lung disease, No. 5; and other consequences of atherosclerosis, No. 9—it is vital that funding be adequate, stable, nonregressive, flexible.

The NHLBI has a demonstrated record of responsible research management. In terms of accomplishments, the productivity of the Institute's basic and clinical research projects, demonstration, prevention, and education programs toward the amelioration of the severe consequences of heart, lung, and blood disorders has been outstanding. As you know, the decline in deaths from heart attack and stroke in the United States, a decline which began in the late 1960's, continued through 1982. It is particularly encouraging the information that Dr. L'Enfant brought to us this morning. The many reasons for this decline all have their genesis in a sustained Federal commitment to research, coupled with creative and careful planning and priority setting under the auspices of the Institute.

The American College of Cardiology believes that for optimal operation of the Institute and in the interest of nurturing the research productivity and preserving the momentum which has been generated over the past decades, extension of the authorization for each fiscal year for the National Heart, Lung, and Blood Institute should be granted on the basis of scientific need and opportunity. The specification of absolute dollar levels has an inherently negative impact, as dollar limits operate in many respects as restrictive ceilings rather than opportunity levels. In the past few years, authorization levels have only minimally exceeded appropriations. We believe this has the potential for the inhibition of research creativity as new initiatives cannot be seriously considered or planned for.

Consequently, the college recommends that authorization be for "such sums as may be necessary" for the National Heart, Lung, and Blood Institute, as it is for all Institutes of the National Institutes of Health smaller in size than the Heart, Lung and Blood Institute.

It must be made clear that we are not recommending a carte blanche for profligate spending, as annual appropriations would require justification as usual. Our recommendation is simply to allow creative research management and the ability to take advantage of unexpected opportunities should they arise.

If the above recommendations for "such sums as may be necessary" is not possible, we propose levels sufficiently high to permit responsible planning for new initiatives and opportunity exploitation. We believe that a 15 percent increase for fiscal year 1984 over the fiscal year 1983 continuing resolution level contained in Public Law 97-377 is responsible. We recommend similar increases for the following 2 fiscal years.

We appreciate your continuing concern for preventive programs to ensure identity for the prevention, education, and control programs of the Heart, Lung and Blood Institute. The college is gratified for the continuation of separate authority and authorization for appropriations for these programs which your bill provides.

A critical problem addressed earlier this morning and one faced throughout the Institutes is that of the dramatic decline of physicians entering careers in academic investigative medicine. If this downward trend is permitted to continue, clinical investigation may become an historical pursuit, and our large investment in biomedical research devalued to an irreversible level.

Several initiatives to encourage clinical investigators have been initiated by the Heart, Lung, and Blood Institute. These include Preventive Cardiology Academic Awards, Clinical Investigator Awards, Research Career Development Awards, minority biomedical support, and minority access to research career programs. We believe these programs are essential, and we are very pleased that the bill preserves them.

In view of the critical role of training in the entire research and research translation process, the college recommends authorization levels of $201 million, $241 million, and $289 million for fiscal years 1984 to 1986 respectively. These levels also will ensure adequate authority to allow restoration of "full institutional allowances." This is another important point.

Consonant with our concern for encouraging clinical investigation as a career, the college favors repeal of the payback requirement under the National Research Service Award program because we believe it unnecessarily inhibits young potential clinical investigators from embarking on research careers. Concern that such awards would be used for subspecialty clinical training alone, concern which prompted the payback requirement, has not been shown to be a serious problem. Certainly, the drastic decline in clinical investigators is a more pressing societal issue. We are pleased your bill addresses this issue.

S. 773 continues the National Heart, Lung, and Blood Advisory Council in its current form. We believe the unique needs of the National Heart, Lung, and Blood Institute require it to be separately authorized, and we are pleased that no revisions were made.

The current statutory composition is preferable to the membership composition proposed in H.R. 1555. Such revision would, in our opinion, further inhibit the ability of the Institute to involve actively an adequate number of individuals with appropriate backgrounds for conducting council business in regard to research. We believe that legislating the number of Council members who shall be experts in particular areas has the potential for interfering with the achievement of balance on issues of scientific substance coming before the Council. The college strongly believes that the chairman of the National Heart, Lung, and Blood Advisory Council should be the Director of the Institute. the college believes that the Directors of individual research Institutes are the most appropriate chairmen. We are pleased that the committee bill retains the language of section 417(d) of the current law.

Section 415 of the Public Health Service Act contains authority for National Research and Demonstration Centers for heart, blood vessel, lung, and blood diseases and resources, which S. 773 continues. Section 415 authorizes 10 centers, each in the 3 traditional areas of responsibility of the Heart, Lung, and Blood Institute. The college believes that the specific designation of 10 centers each for these three areas—heart, lung, and blood—should be amended to authorize 30 centers overall, to give more flexibility. The amendment is recommended to provide the director of NHLBI flexibility in the development of new centers, funds permitting, consistent with the needs, availability and quality of on-going research in the various subject areas under the aegis of the Institute. In addition, the current statutory provisions, in terms of number of centers—10, 10 and 10—are inconsistent with current funding percentages of the research programs of the Institute, which are approximately 66 percent, 17 percent, and 17 percent for heart, lung, and blood areas, respectively.

Concerning the National Library of Medicine, we believe the National Library assistance program provides support for the study, design, development, and improvement of information services for health care professionals throughout the Nation and supports a regional library network which is most valuable. We believe that this program must be stabilized and adequately authorized so that sufficient funds can be provided.

On aspect of this program, alluded to earlier, which must be maintained at its current level of support and expanded considerably in the near future is the library's computers-in-medicine program. Computers today are serving the medical profession in numerous important ways in the diagnosis and treatment of all forms of cardiovascular disease. I am pleased to say that I am a personal recipient of the benefits of this type program in some of the work I am engaged in. It is vital that individuals working in the health sciences be trained in computer technology, and the National Library of Medicine is one of the primary resources for such training.

The college, therefore, is pleased with the authorization level relative to the National Medical Library Assistance Act, which your bill recommends.

The American College of Cardiology hopes that our concerns, comments, and recommendations will be of assistance as you develop this important reauthorization legislation. We are particularly grateful to have been given the opportunity to appear before you today to support your approach for minor revisions of a statute which has worked well in the past and should continue to do so. Our concern is merely to allow adequate research endeavors, and therefore we have made the above-mentioned recommendations on authorization levels.

Thank you, sir. We certainly stand ready to assist in any way we can.

[The prepared statement of Dr. Fox follows:]

PREPARED STATEMENT OF SAMUEL M. FOX III,

INTRODUCTION

I am Dr. Samuel M. Fox III, Professor of Medicine, Georgetown University Medical Center and Director of the Preventive Cardiology Exercise Program at Georgetown University Hospital. I appear before you today representing the 12,000 member American College of Cardiology[1] of which I am a Past President. We appreciate the opportunity to comment on various provisions of S. 773, the "Biomedical Research, Training, and Medical Library Assistance Amendments of 1983," with particular relevance to the National Heart, Lung, and Blood Institute (NHLBI).

It is the opinion of our organization that the performance of the NHLBI has been exemplary under the current statutory authority; and, it is probable that the Institute would continue to perform admirably if the authority were merely extended without amendment, provided sufficient funds were available to allow the Institute to address the many vital issues falling under its broad responsibility. Nevertheless, the College would like to direct your attention to those aspects of the proposed legislation which we believe might be deleterious to the functioning of the NHLBI if adopted, those which might be enhanced in effectiveness through amendment and those with which we are in full agreement as proposed.

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[1] The American College of Cardiology (ACC), a 12,000 member nonprofit professional medical society, is dedicated to ensuring optimal care for persons with or the potential for developing cardiovascular disease, and through education and socioeconomic activities, the prevention of cardiovascular disease.

Authorization of Appropriations

The authorization for appropriations for each Fiscal Year is one issue for which we recommend amendment. As the responsibility of the NHLBI is broad, with four of the ten leading causes of death falling under its jurisdiction -- diseases of the heart (#1), cerebrovascular diseases (#3), chronic obstructive lung disease (#5) and atherosclerosis (#9) -- it is vital that funding be adequate, stable, non-regressive and flexible.

The NHLBI has a demonstrated record of responsible research management. In terms of accomplishments, the productivity of the NHLBI basic and clinical research projects, demonstration, prevention and education programs toward the amelioration of the severe consequences of heart, lung and blood disorders has been outstanding. As you know, the decline in deaths from heart attack and stroke in the United States, a decline which began in the late 1960s, continued through 1982. The many reasons for this decline all have their genesis in a sustained Federal commitment to research coupled with creative and careful planning and priority setting under the auspices of the NHLBI.

The American College of Cardiology believes that for optimal operation of the NHLBI and in the interest of nurturing the research productivity and preserving the momentum which have been generated over the past several decades, extension of the authorizations for each Fiscal Year for the National Heart, Lung, and Blood Institute should be granted on the basis of scientific need and opportunity.

Specification of absolute dollar levels has an inherently negative impact as dollar limits operate as restrictive "ceilings" rather than opportunity levels. In the past few years authorization levels have only minimally exceeded appropriations. We believe this has the potential for the inhibition of research creativity as new initiatives cannot be seriously considered or planned for. Consequently, the College would recommend that authorization be for "such sums as may be necessary" for NHLBI (and the National Cancer Institute) as it is for all other institutes of the National Institutes of Health. If such language were accepted, we would encourage a five year authorization.

It must be made clear that we are not recommending a carte blanche for profligate spending as annual appropriations would require justification as usual. Our recommendation is simply to allow creative research management and the ability to take advantage of unexpected opportunities should they arise.

If the above recommendations for "such sums as may be necessary" cannot be honored, we propose a three year reauthorization with levels sufficiently high to permit responsible planning for new initiatives and opportunity exploitation. We believe the 15 percent increase recommended in H.R. 1555 for FY 1984 over the FY 1983 Continuing Resolution level contained in Public Law (P.L.) 97-377, is responsible. However, we believe this "ceiling height" is the minimally acceptable level. We recommend similar increases for FY 1985 and FY 1986.

Therefore, for the National Heart, Lung, and Blood Institute (other than its prevention, education, and control programs under Section 422), the College recommends the following authorization levels:

FY 1984: $659,000,000;
FY 1985: $756,000,000; and
FY 1986: $865,000,000.

To ensure identity for the prevention, education, and control programs of NHLBI, the College endorses the continuation of separate authority and authorization for appropriations for these programs. Our recommendations assume a 5 percent inflation factor and a 15 percent growth factor. Therefore, for Section 422, we propose:

FY 1984: $57,000,000;
FY 1985: $68,000,000; and
FY 1986: $82,000,000.

Research Training

A critical problem faced by the NIH, in general, and NHLBI, in particular, is the dramatic decline of physicians entering careers in academic investigative medicine. If this downward trend is permitted to continue, clinical investigation may become an historical pursuit and our large investment in biomedical research devalued to an irreversible level.

Several initiatives to encourage clinical investigators have been initiated by the NHLBI. These include Preventive Cardiology Academic Awards, Clinical Investigator Awards, Research Career Development Awards, Minority Biomedical Support and Minority Access to Research Career Programs. We believe these programs are essential and that the bill should ensure that these programs are continued.

In view of the critical role of training in the entire research and research translation process, the College recommends authorization levels of $201 million, $241 million, and $289 million for Fiscal Years 1984-1986, respectively. These levels also will ensure adequate authority to allow restoration of "full institutional allowances."

Consonant with our concern for encouraging clinical investigation as a career, the College favors repeal of the "payback" requirement under the National Research Service Award program, because we believe it unnecessarily inhibits young, potential, clinical investigators from embarking on research careers. Concern that such awards would be used for subspecialty clinical training, a concern which prompted the payback requirement, has not shown to be a serious problem. Certainly the drastic decline in clinical investigators is a more pressing societal issue. We are pleased your bill addressed this issue.

Advisory Councils

Membership

S. 773 continues the National Heart, Lung, and Blood Advisory Council in its current form. We believe the unique needs of the National Heart, Lung, and Blood Institute require it to be separately authorized, and recommend that no revisions be made. The current law requires that: (1) eleven members shall be from among leading medical and scientific authorities skilled in the sciences relating to the mission of NHLBI, (2) two members shall be residents, and (3) five shall be public members who are leaders in the fields of fundamental science, medical science or public affairs. Due to the significantly increased mandate of the NHLBI since 1972, with the addition of lung and blood responsibilities to the National Heart Institute, it has become difficult to achieve an adequate complement of medical and scientific persons within the statutory ceiling of thirteen members.

However, the current statutory composition is preferable to the membership composition proposed by H.R. 1555. Such revision would, in our opinion, further inhibit the ability of the Institute to involve actively an adequate number of individuals with backgrounds most appropriate for conducting Council business. Again, our comments should not give the impression that the College considers the contributions of the disciplines enumerated in H.R. 1555 as unimportant. We believe that legislating the numbers of Council members who shall be experts in particular areas has the potential for interfering with the achievement of balance on issues of scientific substance coming before the Council.

Chairmanship

The College strongly believes that the Chairman of the National Heart, Lung, and Blood Advisory Council (NHLBAC) should be the Director of the Institute. The College believes that the directors of individual research institutes are the most appropriate chairmen. We urge the Committee to retain the language of Section 417(d) of the current law.

NIH Director's Advisory Council

The College believes that this administratively created Council should remain a policy committee without management function or management responsibility.

Contracts

H.R. 1555 would mandate that the Councils of the respective institutes approve all contracts over $500,000. We believe that the NHLBI Council's current responsibilities should not be so expanded. Presently contracts are reviewed by the NHLBI Council on an ongoing basis after awards are made.

At the fourth and last meeting of the NHLBAC in each Fiscal Year, the NHLBI reports on anticipated contract programs for the upcoming Fiscal Year and solicits comments on the Council regarding contracts, priorities, and the percentage of the NHLBI's budget which the Council believes should be allocated to contracts. We believe this activity is appropriate and provides sufficient safeguards.

National Research and Demonstration Centers (NRDCs)

Section 415 of the Public Health Service Act contains authority for National Research and Demonstration Centers for heart, blood vessel, lung, and blood diseases and resources. Section 415 authorizes ten centers each in the three traditional areas of responsibility of the NHLBI. The College believes that the specific designation of ten centers each for these three areas (heart, lung and blood) should be amended to authorize thirty centers overall. The amendment is recommended to provide the

Director of NHLBI necessary flexibility in the development of new centers, funds permitting, consistent with the needs, availability and equality of ongoing research in the various subject areas under the aegis of the NHLBI. In addition, the current statutory provisions in terms of numbers of centers (10-10-10) are inconsistent with current funding percentages of the research programs of the Institute which approximate 66%, 17% and 17% for heart, lung and blood areas, respectively.

Reports

The College believes that the annual NHLBI Director's report should continue to be prepared and distributed. Congress and the public use these documents routinely to assess success in program activities and to recommend statutory and administrative redirection. A biennial report from each institute would be significantly less helpful. We oppose the provision in H.R. 1555 requiring a single, NIH-compiled report, because such report could unintentionally gloss over key intricacies known best by individual research institutes.

National Library of Medicine

The Medical Library Assistance Program provides support for the study, design, development and improvement of information, services for health care professionals throughout the nation, and supports a regional library network. We believe that this program must be stabilized and adequately authorized so that sufficent funding can be provided. One aspect of this Program which must be maintained at its current level of support and expanded considerably in the near future is the Library's Computers-in-Medicine program. Computers today are serving the medical profession in numerous important ways in the diagnosis and treatment of all forms of cardiovascular disease. It is vital that individuals working in the health sciences be trained in computer technology and the NLM is one of the primary resources for such training. The College, therefore, recommends the authorization levels for Fiscal Years 1984-1986 of $10 million, $11 million, and $12 million, respectively, relative to the Medical Library Assistance Act.

The American College of Cardiology hopes that our concerns, comments and recommendations will be of assistance as you develop this important reauthorization legislation. We appreciate the opportunity you have provided us to present our views.

The CHAIRMAN. Thank you so much, Dr. Fox.

We now turn to Dr. Dixon. We are very happy to have you here, Dr. Dixon, from our own university out in Utah.

STATEMENT OF DR. JOHN DIXON, PROFESSOR OF SURGERY, UNIVERSITY OF UTAH SCHOOL OF MEDICINE, ON BEHALF OF THE NATIONAL DIGESTIVE DISEASES ADVISORY BOARD

Dr. DIXON. I am pleased to be here, Mr. Chairman. I am Dr. John Dixon. I want to talk with you for a few moments concerning the authorizing legislation for health research in digestive disease. I am representing the National Advisory Council and a number of coalitions of digestive disease organizations. I just want to say how pleased we are for what this committee has done with regard to getting additional funds overall and for the NIADDK.

My comments relate mostly to a disease center concept as applied to digestive diseases. Although I am billed as professor of surgery, I would like to say a few other things to tell you where my remarks are coming from. I am also a professor of medicine. I am a gastroenterologist. I am the head of an endoscopic and laser surgery unit, a member of many of the digestive diseases organizations. But the other side that I would like to present in my checkered career is that I also for many years was chairman of the State board of health, and elected as city councilman responsible for health, and a member of the board of one of the country's largest private hospital chains, and have been responsible for family, community medicine and public health. So I want to get a broader aspect on this.

How to spend money for research when you have restricted resources? This is the tough problem. We understand that it is a problem you face every day in allocating funds. First, where the greatest number of people are involved, the abused cost/benefit ratio comments, second where the greatest likelihood of prevention as opposed to treatment of end-stage disease might be present, and third where a mechanism exists for organizing and administering research at a level that would be helpful. I would like to speak very briefly to each of these three points as they relate to digestive disease and research.

The first importance of digestive disease—and these statistics are from the National Commission on Digestive Diseases—20 million Americans are involved with chronic digestive diseases; $17 billion in annual direct health care costs result from these illnesses; $50 billion total annual economic costs—time lost, disability payments and so on—result from this disease. Twenty-five percent of all operations in hospitals relate to digestive diseases, and 15 percent of hospital admissions. The staggering impact on the health and economy of our country are evident from disorders of this system complex.

To compare one diseases to others in importance is really not too helpful, but if you add cancer in GI, this is one of the most common causes of a loss of life or loss of health. It is third, if you take cancer out of digestive disease, of which heart, of course, is first and trauma and so on. In a lighter vein, in terms of relative importance, you might be interested in something that my research turned up with regard to comparison. Henry Wheeler Shaw, who evidently was a real representative in the Government about the time of George Washington, summed it up in his comments: "A reliable set of bowels is worth more than any amount of brains."

The CHAIRMAN. I knew we would get some Utah philosophy here.

Dr. DIXON. What about the likelihood of preventive measures and digestive diseases? Can we do anything to prevent? Yes. In ulcers, we have already seen dramatic things in new drugs, such as cymetadine. Sucrafayd is coming along, which will be equally important. In gallstones, it is possible to dissolve gallstones with certain medication, and we working other times on fragmenting stones with ultrasound. The hepatitis, sclerosis, cancer thing has already been mentioned. In my field of endoscopy, we have done over 300 patients this year using an endoscope and a laser to stop bleeding ulcers or remove polyps and tumors and so on, avoiding the necessity for hospitalizations, major operations, and so on. So the possibility for prevention is great;

But what about the mechanism? We are not talking about an institute for digestive diseases, recognizing the organizational situation there. We would support the new proposed institute for the care of senators with ruptured Achilles tendons. We feel that might be a very important one that would be essential.

The CHAIRMAN. I think it is about time.

Dr. DIXON. But we feel very strongly that centers should be established for digestive diseases within the rubric of the National Institutes of Health that would be multidisciplinary. For instance, we are studying a problem in ulcers now, and in that little group we have an endoscopist, an endocrinologist, and pharmacologist, a physiologist, a surgeon, an epidemiologist. They are brought together and their skills compiled in order to deal with these very complex problems.

It is not like prospecting now, where you walk along and the nuggets are all exposed. You have to dig for them, and if you do that, you have to have an organizational structure to bore within, and the centers concept provides that. Second, as has already been emphasized, this provides stable support for investigators so that they can get launched on research, they can interact with other things, and encourage new researchers.

There have been three small centers under NIADDK. Just to show the fate of them, they are funded at $2.6 million the first year, $2.9 million, then $0.5 million, now they are back to $1.2 million. Now that reflects a lot of things, but in the $0.5 million period, a considerable fallout occurred in new investigators, and we feel the centers concept provides some stability. I must point out that this does not provide a pension or an annuity with these people, because they are peer reviewed and then they have to go out and compete on an individual basis, but it does get them started.

In summary, the NIADDK is doing a great job. The NIH is doing a great job, and we appreciate your support of them. But we feel that the special problems relating to digestive disease require special interests, and we finally believe that the best investment in health research is through research. Under that, we feel that the digestive disease component, research centers most expeditiously bring together a group that helps prevent this disease, and we would like to back them up with a data collection mechanism which would provide information for their activities.

Thank you very much. I will be happy to respond to questions or comments.

[The prepared statement of Dr. Dixon follows:]

PREPARED STATEMENT OF JOHN DIXON

Dear Mr. Chairman:

Thank you for the opportunity to speak to you and members of your committee on behalf of the National Digestive Diseases Advisory Board. As you are aware digestive diseases represent one of the Nation's most serious and financially burdensome health problems. The National Commission on Digestive Diseases indicated that hope for progress towards the alleviation of this burden lies largely in biomedical research specifically targeted for digestive diseases. They recommended that research be supported by individual research grants, but indicated that for certain problems the most efficient and effective approach is through the development of centers for digestive diseases.

In its 1979 report to Congress, the National Commission on Digestive Diseases first assessed the burden of digestive tract illness; they found that:

> "Digestive Diseases constitute the third largest component of the total economic burden of illness in the United States, being outranked only by circulatory diseases and by the combined category of accidents, poisonings and violence."

The commission made an intensive study and provided an extensive report on opportunities for research in digestive diseases. This report has been reguarly updated by groups such as the Digestive Diseases Coordinating Committee. New opportunities have been recognized as advances in technology on concepts made them possible. A few of these opportunities are described in the attached material.

The report also addressed four basic questions concerning centers and specialized facilities. These questions are:

1. Should there be an increase in the number and/or funding levels of research Centers in digestive diseases?

2. What digestive disease areas might be approriate for Center research?

3. What types of Center vehicles (e.g., CORE Centers, Specialized Clinical Centers) are best suited to the needs in the area of digestive diseases?

4. What factors should be considered for the establishment of a Center?

The conclusion reached in the report stated that there should be an increase in the number and funding levels of research Centers in digestive diseases. NIADDK through internal allocation of funds at that time funded research centers in liver disease and peptic ulcer disease. The report strongly recommended increases in funding for center efforts in these specific disease areas. In point of fact, the dollar allocation specifically for centers for Digestive Diseases was $2,315,000 in 1978; $2,974,000 in 1979; $2,953,000 in 1980; $533,000 in 1981 and $1,467,000 in the President's budget for 1982. This latter figure represents support for the two research liver centers. There is at the present time no specific center support designated as such for the peptic ulcer research center in California.

In summary then (and in contrast to the National Commission's recommendations) the support for digestive diseases centers has diminished and today there are only two centers devoted to digestive diseases research and these centers are supported by internal allocation of NIADDK funds which as you know is becoming an increasingly more difficult situation because of budgetary constraints.

Furthermore, a review of the pertinent sections of the National Commission's report and of the implementation of its provisions shows that only minor progress has been made in the past three years in the areas of epidemiology research and training, nomenclature, environmental and occupational toxins.

The National Digestive Diseases Advisory Board decided early at its meetings to focus on two of the issues addressed by the commission, namely, Digestive Diseases Centers, and an epidemiology and data systems specifically for digestive diseases.

I will first address the issue of centers for digestive diseases.

Centers provide an unique opportunity for interdisciplinary and collaborative research where basic scientists can interact with clinical scientists and clinicians to effectively investigate a major disease problem. This concept is evident in the accomplishments of the two current liver centers and the peptic ulcer center.

The National Commission's report on centers also states that "inflammatory bowel disease and pancreatic diseases are areas which might soon become appropriate for Centers, as recent basic science developments have provided a platform from which an assault on the diseases of these organs could be effectively launched".

The Commission workgroup at the time of there report did not consider "a high priority is due at this time of research in other digestive disease areas". However, periodic review of the need for Centers was considered important, "as the disease problems and research "state of the art" change in digestive diseases." The National Digestive Diseases Advisory Board now unanimously recommends the establishment and development of a Centers program for digestive diseases. This recommendation is based in part on a review of the research progress made in other centers (e.g., diabetes and arthritis, as well as the existing NIADDK liver and ulcer centers); a review of the research accomplishments, advances, and research opportunities in government agencies as prepared by the Digestive Diseases Coordinating Committee; and review of the potential opportunity for research collaboration prepared for the Board by the directors of the NIAAA, NIA, NIAID, and NICHHD. These research accomplishments and advances are listed in the annual reports prepared by these organizations and form part of the testimony which you will hear from other groups and organizations. Therefore, I will focus my remarks on the opportunities for research through the centers mechanisms of the NIH and the opportunities for collaborative efforts directed towards digestive diseases research.

There are investigators able to lead centers in areas such as endoscopy, transplantation, pancreatic disorders, and inflammatory bowel disease. The program staff at the NIH however, has been reluctant to encourage the development of proposals for such centers in the absence of a legislative mandate and in the absence of specific incremental dollar appropriations for centers in digestive diseases.

The value and effectiveness of centers programs in other biomedical fields e.g. arthritis and diabetes, is demonstrated by several salient facts. For example, an analysis of the scientific program of the American Rheumatism Association for 1979 revealed that 34 percent of its research papers emanated from the 24 Multipurpose Arthritis Centers; A survey of the scientific program of the 1979 annual Arthritis Health Professions Section Meeting showed that 67 percent of the research papers presented came from the Multipurpose Arthritis Centers. It is also noteworthy that both of these two scientific meetings saw the largest number of papers submitted and accepted in the history of the American Rheumatism Association and Arthritis Health Professions Sections of the Arthritis Foundation. Also, by way of example, experience with the the diabetes research and training centers indicates that of the more than 100 pilot studies that were supported by these centers, ninety-two percent of the principle investigators so supported have subsequently applied for independent support. Of those who did apply, fifty percent successfully obtained independent support from the National Institutes of Health; 35 percent applied for support and were approved but not funded; 10 percent received funding from other peer-reviewed sources; and seven percent are currently under review.

I will note here that the effectiveness of each of the center programs is regularly monitored by peer review and that the renewals of each center is on a competitive basis for 3-5 years of support.

Additional evidence of research productivity is provided by the information that over 25% of the papers and poster demonstrations presented a the National Scientific Meeting of the American Diabetes Association in June 1981, were by investigators from diabetes centers.

At the present time there are three units in the digestive diseases program activities which are devoted to research and which provide contributions to research comparable to those of the centers in arthritis and diabetes. These centers (a peptic ulcer center and two liver research centers) offer and have provided the types of advantages to the biomedical research which are present in the congressionally authorized and supported centers in arthritis and diabetes. However, the budget for the digestive diseases program is much smaller than the arthritis and diabetes program and it has had no opportunity to expand its centers activity because of limited funds. All though these centers have resulted in interdisciplinary research and research productivity, the digestive diseases Centers Program has not had the major impact on the field that the diabetes and arthritis centers have had.

A draft of the legislation which was unanimously endorsed by the National Digestive Diseases Advisory Board provides for the establishment and development of new digestive diseases centers. These new centers could address and focus upon research in the areas of digestive diseases outlined in the 1979 Congressional Report by the National Commission on Digestive Diseases.

It is apparent from the progress made through the use of centers in research focused on arthritis and diabetes, that the congress and the public can expect similar progress in areas of digestive diseases research also through the use of centers specifically designated, and funded for digestive diseases.

Let me now turn to the second issue, that of epidemiology and data systems for digestive diseases. Here again the experience with the arthritis and the diabetes programs is instructive and useful. Those programs have incorporated where feasible and useful population studies in centers wherein the grant mechanism is "institutionalized" and is independent of the investigators. Thus, long term studies are possible in order to follow developmental aspects of diseases and disorders, and to control and measure the impact where possible, of new technologies, of methodologies, and of medical interventions. Clearly, a dedicated data processing system for clinical data on digestive diseases is needed (it does not exist at the present time). This system could be used to collect population-based total inpatient and outpatient digestive diseases statistics. It could also be used to assist in the assessment of the social and economic impact of chronic digestive diseases and could be used to measure the full impact of digestive diseases on Medicare expenditures. Large benefits should be obtainable at relatively modest cost through population-based controlled studies in digestive diseases.

Mr. Chairman, in conclusion I will reiterate to you the diversity and the nature of digestive diseases. Digestive diseases vary in severity from brief, self-limited illnesses to chronic, disabling, and significant numbers of fatal conditions. Their total social and economic impact is enormous. Measured in terms of morbidity, motility, and cost, they constitute the third largest component of the total economic burden of illness in the United States.

If cancer of the digestive system and its associated organs which account for 25 to 30 percent of cancer deaths are included in the economic burden that these diseases represent, the cost to the public, and the burden on the individual is the most serious in the United States today. Digestive diseases continues to represent the leading cause of hospitalization, 10 percent of the total economic burden of illnesses in the United States, and the primary reason for surgery.

Thank you for the privilege to appear before you. I will be happy to respond to questions or comments.

RESEARCH OPPORTUNITIES

- Research Opportunities Made Possible Through The Development of Endoscope Technique

Over the past 25 years we have developed instruments that contain flexible glass fibers through which we can look directly inside the gastrointestinal tract and see ulcers in the stomach, or polyps in the colon instead of looking for their shadows on an X-ray. These instruments greatly altered the practice of gastroenterology.

The available technology offers possibilities for major advances, if not a revolution, in gastroenterologic research. We may be able to study clinical problems directly in those patients with disease, rather than relying on inferences from studies in test tubes or experimental animals.

- Ulcers and the Circulation in the Digestive Tract

Knowledge of the circulation is important to our understanding of, and ultimately the treatments of, several disorders. For instance, stress related erosions of the stomach and upper intestine may bleed and lead to death in patients who are already dangerously ill. In these patients, evidence suggests that the stomach and intestinal wall may be vulnerable to erosion because of impaired circulation.

Such knowledge may also be important to our understanding and development of a treatment for the more common forms of peptic ulcer. These ulcers occur in people who are otherwise well. While the ulcers usually heal, it is common for another ulcer to form within several months to a few years, and the recurrent ulcer is often found at the same spot as the first ulcer. Evidence suggests that healing may leave an altered vascular pattern. Knowledge of the vascular changes during the formation and healing of ulcers could lead to a better understanding of the factors that cause ulcers and hopefully lead to improved treatment and perhaps help prevent the recurrence of this common digestive disorder. In some cases, blocks occur in blood vessels supplying blood to a part of the intestine. The ability to measure the circulation in segments served by the blocked vessel would provide a basis for a surgeon's decision as to whether to operate, and if so, what segments to remove.

° Gallstones, Cause and Treatment

Another series of opportunities for research results from the ability to put a catheter into the small biliary ducts and obtain bile close to the sites where it is formed in the liver. It is likewise possible to obtain successive samples of bile as it passes on down through the larger ducts that finally drain into the gallbladder and then into the intestine. Such samples should provide precise information on the bile as it is formed and changes that occur as it passes down the ducts, with the hope that the insights to be gained from this will provide further useful information on the causes of and treatments for gallstones. We may be helped in these studies by devices, like the catheters, which can be introduced well up into the ducts and have at their tips, sensors which can measure the concentrations of such substances as carbon dioxide, calcium ions, and hydrogen ions.

Using catheters, we can introduce substances which dissolve gallstones, into the ducts and study how and why they work, and what their limitations are.

° Pancreatitis

Possibly as important, or even more important, is the opportunity to study the pancreatic secretion in the pancreatic ducts. Pancreatitis is a common disorder that can be fatal, and in many cases becomes disabling because of frequent recurrences which ultimately may destroy the pancreas. Pancreatitis is associated with alcoholism, biliary tract disease, and high fat levels in the blood. We do not know how any of these disorders cause pancreatitis. The pancreas has been very difficult to study. Until recently we could not abstract pure secretions from the pancreas, but could only obtain the pancreatic juice after it had passed into the intestine and had become contaminated with intestinal contents. With the use of the endoscope we can now obtain pure secretions near the site where it is secreted, and also observe changes in its composition as it passes down the ducts. We already know there are some important changes and stones may even form in the ducts. It may be possible to observe the effects on pancreatic secretion of alcohol, of high blood fat, and of biliary tract disorders, and translate these observations into better understandings which ultimately may lead to treatment and therapy for this disease.

- Interaction Between Hormonal Effect in the Brain and Gut

Recently scientists have found a number of hormones that regulate secretion movement, cell growth, and cell regeneration in the gastrointestinal tract. Even more recently, they have found some of these same hormones, such as cholecystokinin and gastrin, in the brain. We now want to determine the reasons why these hormones are found in both the brain and the gut. It may be that a common cause of digestive problems during mental or emotional stress is due to the release of hormones from the brain and these same hormones are then responsible for the changes in secretion or motility eventuating in clinical symptoms. These hormones have a variety of functions in brain and gut. For example, in the gut cholecystokinin causes the gall bladder to contract and the pancreas to secrete. In the brain the hormone may regulate appetite. Gastrin (another hormone) in the stomach causes secretion of acid. When applied to certain sites in the brain, gastrin may also induce the stomach to secrete acid.

We are synthesizing, purifying, and even isolating the hormones from human sources, and not just from animals, as in the past. Basic scientific studies using these hormones should generate knowledge leading to a better understanding of brain-gut interaction.

- Chronobiological Factors in Digestive Function & Disease

Data has been accumulated over the past 20 years suggesting a considerable impact of biological periodicities on clinical, diagnostic, and therapeutic schedules. Naturally occurring rhythms affect the morphology and function of the digestive system, as well as the secretion of hormones, response to drugs, and resistance to toxic agents. These observations suggest that future research should consider the effect of the time of day or the season on digestive tract function. Variations in enzyme activity influence the effectiveness or toxicity of the drugs we give, and it may be important to time the administration of drugs to reduce potential side effects. Further, there is the possibility of measuring changes in common, naturally occurring rhythms to detect the early onset of gastrointestinal disease or to anticipate attacks of several diseases. For example, if individuals were to determine their own normal rhythm pattern for simple variables such as body temperature, pulse rate, blood pressure, or grip strength, it might be possible to identify specific alterations that predict the onset of the active phase of a disease. With such information physicians could begin treatment before severe symptoms develop, and could thus minimize the discomfort of the patient, improve the efficiency of the treatment, and even reduce the amount of hospitalization required.

• Nuclear Changes in Patients with Chronic Hepatitis Who Develop Cancer of the Liver

Recent advances have made it possible to detect very small amounts of the viral material from the hepatitis B virus. With these tests, viral material can be detected in liver samples weighing 10 to 20 milligrams. This size sample can be obtained by needle biopsy of the liver.

Studies suggest that there may be progressive damage in some patients who are asymptomatic carriers of the hepatitis virus. Initially after infection, the nuclear material from the virus is present in the liver cells, but not in the liver cells' nuclei. This observation remains true over the short term. However, after several years it has been possible to detect viral nuclear material in the nuclei of the liver cells themselves. Importantly, the viral nuclear material may become imbedded in the chromosomes of the chronically infected patient. This incorporation of the viral material into the liver cell nucleus has been associated with cancer of the liver. This suggests a possible mechanism by which cancer of the liver may develop as a result of a viral infection. The study also provides an impetus to further the use of the hepatitus B vaccine. It is possible that vaccination against hepatitis B could alter the incidence of cancer of the liver. This is the most common cancer in the world as a whole, though it is not among the common cancers in the United States.

• A Clinical Trial of Endoscopic Treatment of Upper Gastrointestinal Hemorrhage

Gastrointestinal bleeding is an important medical problem accounting for at least 150,000 hospital admissions each year in the United States. Despite improvement in the overall care of critically ill patients and the ability to diagnose bleeding lesions by endoscopy, the mortality of patients with significant GI hemorrhage remains at approximately 10%. Older patients are at increased risk, and the proportion of patients over age 60 with bleeding has increased significantly (from 8% in 1937 to 45% in 1976). The frequency of death is high if hemorrhage has to be treated by abdominal surgery. Altefnative procedures are urgently needed.

It is now possible to see the site of bleeding through an endoscope. Early work suggests that cauterizing the bleeding site through the endoscope will stop the bleeding. If this treatment should prove to be successful, we could avoid the special risk of abdominal surgery in those patients who are often critically ill.

- Cirrhosis - Opportunity for Preventive Therapy

Cirrhosis is the term used to describe the result of any illness affecting the liver which heals with chronic scarring of the liver. This illness is more common than generally recognized. It now ranks seventh amoung causes of mortality. Most diseases which will eventuate in cirrhosis do so in a slow but relentless fashion. Gastroenterologic investigators are actively pursuing research into the biochemical basis of the scarring process. There is now an opportunity to study agents which may interfere with and halt the scarring process. Some of these agents have already reached the level of clinical trials and offer a potential for preventive therapy in major form of liver disease.

- Sucralfate - A new approach to study the process of ulcer healing

The last five years have seen a revolution in the therapy for peptic ulcer disease. We had been depending primarily on antacids which neutralize the stomach acid responsible for ulcers. Recently, other safe and effective drugs have been developed. The first of these is cimetidine. This agent is capable of suppressing 90% of the stomach's acid secretion and heals ulcers more rapidly than do antacids. Further, if the patient continues to take the medicine, the ulcers are less likely to recur.

A new agent, sucralfate has recently been approved by the FDA. This agent works in an entirely different manner from either antacids or cimetidine. The drug is bound six times more avidly in areas of ulceration than in surrounding normal tissue. It works by producing a chemical terpaulin over an active ulcer and thereby promotes healing. Pepsin activity, which enhances the damaging effects of acid, is also inhibited by this drug. A recent study shows sucralfate to be as effective as cimetidine in promoting healing. Importantly, because this new agent acts differently than other anti-ulcer agents, it may work when other agents do not, or it may be that combination therapy, independently attacking the problem on two fronts could be more sucessful than any of the drugs used alone.

* Pigment Stones

Gallstones are a distressing, common, but to date a difficult to manage illness. The therapy has historically been surgical, but there are now oral medications which can be of use in some patients with cholesterol stones, the most common type of gallstone. Another type of gallstone, pigment gallstone, comprises 27% of gallstones. As yet, there is no medical therapy for these stones. We have, however, identified factors which render patient's more suceptible to pigment stones; for example, patients with increased rates of red cell destruction such as sickle cell anemia. We are now beginning to understand the factors involved in pigment stone formation. The physical-chemical nature of pigment stones is unfolding. First, pigment stones appear to be polymeric in nature rather than being a hydrated crystalline form - as is the case with cholesterol stones. It is also recognized that the pigment group may be subclassifiable. New data suggests that pigment stones are neither chemically nor clinically homogeneous. The follow-up of similar leads in studies of cholesterol stones lead to clinically useful drugs, and, for now, the pigment stone work is moving in the same direction. Determining the solubility properties of this type of stone should not only shed light on this fundamental disease process, but could also lead to the development of drugs similar to those used effectively to dissolve cholesterol gallstones.

- Liver Transplants

Hepatic transplantation is not a new idea, but for a number of reasons has remained a very uncommon therapy for chronic and acute liver failure. Many of the early surgical problems seem to be resolved and certain new adjuvant drugs, especially cyclosporin A, have resulted in improved control of post-transplantation rejection problems. The most recent survival figures are very encouraging and there are patients living as long as nine years following a liver transplant. It is estimated that for the 5000 potential candidates for such therapy, there exists a donor pool of 12 to 60 thousand donors. Hence, organ availability does not now seem to be a a limiting factor. Because of the special needs and surgical skills required, this is one area which could benefit from the establishment of one or more liver transplant centers. At present, a center would be most likely to provide the optimum of clinical care while continuing to provide quality research at a cost-effective level.

The CHAIRMAN. Thank you very much, Dr. Dixon.

Dr. Engleman, we will turn to you now.

Dr. ENGLEMAN. Thank you very much, Senator Hatch. We have submitted a statement, and I would hope that would be included in the permanent record.

The CHAIRMAN. All of your statements will be included in the record as though fully delivered. I might mention that we will keep the record open for all Senators on this committee to submit written questions, and we hope that you can respond to those as quickly as you can. Senator Quayle in particular has been here through these hearings. He had to leave, but he has a set of written questions that he will submit, and we hope that you can respond as quickly as you can.

STATEMENT OF DR. EPHRAIM P. ENGLEMAN, DIRECTOR OF THE ROSALIND RUSSELL MEDICAL RESEARCH CENTER FOR ARTHRITIS, UNIVERSITY OF CALIFORNIA

Dr. ENGLEMAN. Senator, my name is Ephraim P. Engleman. I am a practicing physician and clinical rheumatologist, clinical professor of medicine, and director of the Rosalind Russell Medical Research Center for Arthritis at the University of California in San Francisco. I am president of the International League Against Rheumatism, and formerly president of the American Rheumatism Association. I was chairman of the National Commission on Arthritis and Musculoskeletal Diseases which, pursuant to legislation starting in this committee, developed the National Arthritis Act in 1976.

I appear today on behalf of the Arthritis Foundation, which is the only national voluntary organization of lay and professional supporters of research and education on arthritis. More particularly, I speak for the 37 million American sufferers from arthritis who need and deserve the creation of a National Arthritis Institute in the NIH.

It was my privilege in 1981 to testify in a hearing on arthritis conducted by Congressman Claude Pepper. The title of the hearing was, "The War on Arthritis: When Does It Begin?" In my opinion, the question is still relevant.

In the United States today, arthritis is found in one out of every seven people. It is the most widespread, crippling, disabling, and often most painful of all chronic diseases. There is hardly an American family that does not have at least one member with some form of arthritis. As you know, arthritis is not a single disease. It is a group of more than 80 disorders, which may affect not only joints, bones, and muscles, but also the kidneys, lungs, skin, eyes, blood vessels, and even the brain. And, Senator Hatch, you will be interested to know that it also may involve tendons.

Some of the commonest forms of these disorders include osteoarthritis or degenerative joint disease, rheumatoid arthritis, osteoporosis, and many others. Most forms of arthritis are seen in middle and old age. Four percent of our population over the age of 65 have some form of arthritis. As our population grows older, the prevalence of arthritis will inevitably increase. Nevertheless, it is noteworthy that 250,000 of our children have arthritis, a prevalence rate higher than that of polio during the most severe epidemic of the past.

The financial burden of arthritis is devastating. The National Center for Health Statistics projects that in the year 2000, less than 20 years from now, the cost of arthritis in this country will approach $100 billion.

The Congress showed remarkable foresight when, in 1950, it created an institute which would conduct and support research and research training in arthritis and allied diseases. That institute was called the National Institute of Arthritis and Metabolic Diseases. But what has since happened to that institute? For many reasons which were not necessarily scientific, but often convenient, the institute has been assigned with additional responsibilities for research and research training in such disparate and basically unrelated diseases as diabetes, digestive diseases, kidney, and neurological diseases, nutritional disorders, blood, and endocrine diseases. The old NIAMD is now the Institute of Arthritis, Diabetes, Digestive, and Kidney Diseases [NIADDK]. We may soon run out of letters with which to designate this organizational hodgepodge.

The **Chairman**. Not in this town. We go by acronyms all the time. It is a totally different language.

Dr. **Engleman**. Little wonder why fiscal support of research in arthritis has been lost in the shuffle. The recent elevation of the institute to bureau status has not and will not result in any programmatic improvement, nor will it resolve the funding imbalance between arthritis and other research programs of the NIH.

Fiscal year 1982 appropriation for arthritis was approximately $69 million, less than 20 percent of the total appropriation for the institute. It represents about 1 percent of the total funds awarded to the NIH or less than $2 for each arthritis patient in the United States—a pittance of support for research in the commonest of our chronic diseases. Support of arthritis research is less than one-half the amount recommended by the Arthritis Commission.

This does not mean to imply that we have not made significant progress in our understanding of these disorders. Clearly important and exciting investigations, especially in genetics, virology, immunology, and biomechanics have resulted in major advances in our knowledge of disease mechanisms. In the meantime, however, treatment is still largely dependent on the use of symptom-relieving drugs, physical techniques such as directed exercises, and orthopedic surgical procedures. With rare exception, we have no cure, we have not yet discovered the cause, and we have no mention of prevention.

The time has come to assign a special priority to provide better focus and support for research in arthritis. Indeed, the reasons for establishing a new research institute for arthritis are compelling. The institute will provide a unified purpose. It will facilitate research in surgical and rehabilitative, as well as biomedical problems relating to arthritis, a functional grouping of activities that make sense for our patients and addresses the problems of our patients. It will provide best the visibility, the flexibility, and leadership so vital to the generation of support for the required research program. It will center of targeted biomedical and biophysical approaches which, in the case of arthritis, comes at a particularly propitious time.

The magnitude of the problem and the existing opportunities dictate the need for this new institute. Will the creation of this institute require large amounts of administration funds which will significantly divert funds from research? We think not. Unlike other newly-organized institutes which started from point zero, the new institute will have the benefit of the current arthritis division of the NIADDK, its program staff, and its preexisting allocation of salaries and expense funds. These can readily be transferred to the new institute.

Will in fact a new institute of arthritis substantially stimulate research? One has only to look at the recently created Eye Institute and the Institute of Aging, for which favorable legislation was strongly resisted by the administration. The programs of both institutes have shown a degree of productivity which far exceeds that which might have been anticipated had those same programs remained as parts of a larger institute. In both instances, separation from the larger institute provided the previously-lacking critical ingredient of leadership to a field of research at the national level.

In summary, Mr. Chairman, we believe this is the right time to establish a National Institute of Arthritis and Musculoskeletal and Skin Diseases. We believe the bill to accomplish this is timely and appropriate, in light of the magnitude and complexity of the issues relating to arthritis, and in view of the need for national visibility and leadership to deal effectively with these issues and problems. On behalf of the Arthritis Foundation and the millions of arthritis patients and their families who will benefit from research and treatment, I urge prompt enactment of legislation to create this new institute. Thank you very much.

[The prepared statement of Dr. Engleman follows:]

STATEMENT
OF THE
ARTHRITIS FOUNDATION
BEFORE THE
COMMITTEE ON LABOR AND HUMAN RESOURCES
UNITED STATES SENATE
ON S. 773, HEALTH RESOURCES ACT OF 1983

March 17, 1983

Mr. Chairman and members of the Committee, my name is Ephraim P. Engleman, M.D. I am a practicing clinical rheumatologist, Director of the Rosalind Russell Medical Research Center for Arthritis, University of California, and was Chairman of the National Commission on Arthritis and Musculoskeletal Diseases which, pursuant to legislation originating in this Committee, developed the National Arthritis Plan in 1976.

I appear today on behalf of the Arthritis Foundation, the only national organization supporting research and education with respect to all forms of rheumatic disease. The Foundation's work is supported through the efforts of some 400,000 volunteers across the country. Most particularly I speak for the millions of Americans suffering from arthritis who want and need the creation of a National arthritis institute in NIH.

We now estimate that 37 million of our people are victims of arthritis. Within that broad diagnostic category are 100 distinct disease entities, ranging in scope and severity from scleroderma to gout, to ankylosing spondylitis, lupus and rheumatoid arthritis.

Mr. Chairman, the Arthritis Foundation appreciates the opportunity you have afforded to us to speak on behalf of the provisions of S. 773 establishing a National Institute of Arthritis, Musculoskeletal and Skin Diseases. We are aware of this Committee's longstanding and continuing interest in biomedical research, and of its recognition of the vital importance of such research to the health of all Americans. The National Institutes of Health is the foremost research institution in the world, and its preeminent position must be preserved. This Committee has been in the forefront of this vital cause.

We are pleased to note that the Chairman of this Committee is an original co-sponsor of S.540, the legislation introduced in the Senate to establish an Arthritis Institute. Arthritis is the nation's number one disabling disease. The number of Americans with arthritis is increasing by a million victims every year. Although arthritis and musculoskeletal diseases affect all ages, 40 percent of the population over age 65 has a rheumatic disease. As our nation's population ages, the prevalence of arthritis will inevitably increase. It is projected that the elderly population will grow from 10 percent of the population to 20 percent by the year 2030.

Some 250,000 of our children have arthritis, more than the number of young people who contracted polio during the most virulent outbreak of that disease.

The National Center for Health Statistics projects that in the year 2000 -- less than 20 years from now -- expenses attributable to arthritis will reach nearly $100 billion.

Mr. Chairman, it is clear that arthritis is serious, widespread, and terribly expensive. It is equally clear that we are doing far too little as a nation to reduce its impact.

The section of S. 773 creating a new arthritis research institute, along with S.540, which has been referred to this Committee, are but the latest steps in an evolutionary process that began in 1950 with the creation of the National Institute of Arthritis and Metabolic Diseases. Although rheumatology was barely a recognized subspecialty at that time, and research in rheumatic diseases was rudimentary, this first national recognition of the need to unlock the mysteries of this congeries of diseases spurred an interest in the field that has since constantly accelerated. By the late 1960's there had surfaced substantial public expression of the need for greater attention to arthritis research, and by 1974 Congress had enacted the National Arthritis Act. That legislation and the resultant National Arthritis Plan developed by the National Commission on Arthritis and Related Musculoskeletal Diseases, which I was privileged to share, represented the first comprehensive national assessment of the status of biomedical research in arthritis and rheumatic diseases; the level of care being provided to arthritis patients; and the structures and mechanisms that should be created or improved in order to give proper attention to a massive national health problem.

The National Commission set forth some 150 specific recommendations which it believed should be addressed in order to adequately promote a national attack on arthritis. The essence of the Commission's findings is that the vast impact of arthritis on the nation has not been matched by a determination to accelerate research and training to improve the treatment of rheumatic diseases, to prevent them, and to find cures for them.

Although some progress has been made in addressing the Commission's recommendations since the publication of the National Arthritis Plan in 1976, a great deal remains to be done. The National Arthritis Advisory Board was created, Multipurpose Arthritis Centers were initiated, and a modest arthritis data base has been established. Funding recommendations in the Plan have not materialized. Less than half the amounts urged for research have been made available. Although epidemiology studies are critical to understanding the origins and demography of arthritis, next to nothing has been undertaken in this vital field.

The amount of research in arthritis has been pitifully small in contrast with the need. Many promising discoveries in recent years have led to our firm belief that, in time and with adequate support, some forms of arthritis might be prevented, cures may be found, and surely, therapies can be improved. The isolation of genetic markers for ankylosing spondylitis, hormonal involvement in systemic lupus erythematosus, and the identification of the inflammatory processes in rheumatoid arthritis are among those scientific discoveries made in recent years.

So much more can be done. And with the proper environment, focus, and support we can and will build on these exciting and promising recent accomplishments.

Mr. Chairman, we believe strongly that the time has come to assign a special priority to research on arthritis and musculoskeletal diseases. The reasons for establishing a new research institute for this purpose are compelling.

As I have indicated, arthritis is not a single disease but many. There are at least one hundred different diseases classified as rheumatic, each with its own causes, symptoms, and treatment modalities. In addition, musculoskeletal diseases such as scoliosis and kyphosis in children, and osteoporosis in the elderly are proper subjects of study by a single institute. This vast panorama of illnesses cannot be investigated adequately in an institute whose fields of study are so diffused and unrelated.

The magnitude of the human and economic impact of arthritis on the nation, along with the expectation that its prevalence will constantly increase, demand a sharp national focus on this family of diseases that only a separate institute can bring. Arthritis and other musculoskeletal diseases are responsible for major costs of workers' compensation, social security benefits, medicare payments, and hospital and nursing home stays. Nearly $1 billion annually is spent by arthritis sufferers on quack remedies and unproven drugs and treatment.

The Arthritis Foundation strongly disagrees with the assertion of the Administration that the creation of the proposed institute would divert funds away from the arthritis research program and the total NIH research effort. Although some minimal level of additional administrative costs would be incurred, the amounts cited by NIH are unrealistically high. The Arthritis Division of the National Institute of Arthritis, Diabetes, and Digestive and Kidney Diseases has program staff and its own allocation of salaries and expenses funds. During this time of fiscal constraint, many administration and management functions can be shared, with no additional personnel required for those functions.

To place this issue in proper context, it is important to keep in mind the cost to this country of arthritis and musculoskeletal diseases. Twenty times as much is spent on quack cures as is expended for research. Many billions more are lost to the economy due to medical expenses, disability benefits, lost wages and taxes, and workers' compensation payments.

Mr. Chairman, the report of the National Commission on Arthritis and Related Musculoskeletal Diseases, entitled "Arthritis: Out of the Maze" includes a statement, the validity of which is as strong today as it was six years ago. That passage bears repeating:

> "It is incongruous to include under one organizational umbrella such disparate and basically unrelated diseases as arthritis and diseases of the bone, diabetes, digestive diseases, kidney and urological diseases, skin disorders, problems related to nutrition, metabolism disorders, blood diseases and endocrine diseases. The establishment of a separate institute directed specifically toward the problems of arthritis would have clearcut advantages as indicated by the other institutes specializing in a single or logically grouped family of disorders. It would attract the best possible leadership and result in a higher quality research program. It would tend to focus on targeted biomedical approaches, and in the case of the arthritis diseases, this comes at a particularly propitious time."

Mr. Chairman, we believe, and earnestly hope this Committee agrees, that the justifications for establishing a National Institute on Arthritis and Musculoskeletal Diseases are compelling. We believe, further, that the case for establishing such an institute is much stronger than that of any other field because of the number of victims, the number of diseases, and the state of research science in the field. Eight years have passed since the most recent NIH research institute was created. The current structure and alinement is not, and should not be, sacrosanct. Other organizations interested in NIADDK research agree that now is an appropriate time to examine the efficacy of reconstituting NIADDK programs.

During the last Congress both the House of Representatives and the Senate passed legislation to create a new National Institute of Arthritis and Musculoskeletal Diseases. Unfortunately, time ran out before an agreement could be reached and the bill sent to the President.

This year, Mr. Chairman, we are gratified that the Congress is continuing the work it began in the 97th Congress. Both your bill, S. 773, and the counterpart House legislation, H.R. 1555, the Health Research Extension Act of 1983, now pending before the House Energy and Commerce Committee, include provisions for a new arthritis institute. We commend both bodies for your interest and enthusiasm in this important matter.

On behalf of the Arthritis Foundation and the millions of arthritis sufferers and their families who would benefit from advances in research and treatment, I urge the prompt enactment of legislation to create a National Institute on Arthritis and Musculoskeletal Diseases.

That concludes my statement, Mr. Chairman. I will be happy to respond to any questions the Committee may have.

The CHAIRMAN. Thank you, Dr. Engleman. We appreciate the testimony that all four of you have given here today.

Dr. Talbot, we know that Fox Chase has provided a great deal of leadership in the area of cancer research and treatment, thanks in large part to your leadership over the past 25 years.

Could you just answer this for us. With all the money we put into cancer research, I think, unlike many people who may not have looked into this as much as I have, we have had some remarkable changes in the success ratio. But still, let me ask this question. With all the money we have put into cancer research over the last number of years, do you have any reason why we have not increased the percentage of successful cancer prevention and cure beyond where it is today?

Dr. TALBOT. I am glad you said "beyond where it is today," because it is not where it was. It is much better than it was, as you are well aware.

The CHAIRMAN. I look at the 50 percent success rate with regard to leukemia, for example, and that is an amazing achievement. Of course, we would like to see a 100 percent success rate.

Dr. TALBOT. Yes. As both Dr. DeVita and others have testified here before, they have given statistics that I realize the committee already has so I will not repeat them. Surely, we have made vast improvements and advances over what we had 20 or more years ago. It is a different world, a totally different world than it was then. It is much better. But the way in which I tried to speak, about the accumulation constantly and consistently of a reservoir of fundamental scientific, biomedical knowledge is at the root of all of these advances. We will perhaps wake up some day and find that there will be some dramatic single cause discovered for some or perhaps even all of these problems. But it is going to come through the kinds of studies that are based on a growing pool and flowering, as I have said, of the fundamental aspects of biological knowledge. That, it seems to me, is what we now see coming into bloom. It seems also to me and to all of us that this kind of nurturing and feeding of that kind of effort, so that it does not fall back, is where we will get our future advances. I have great faith that those will happen if we continue in that path.

The CHAIRMAN. Thank you so much. Dr. Fox, I am going to submit some questions to you for the record, but one of the things I wondered about in your testimony is this. I understand that the actual number of M.Ds choosing careers in research has been approximately level since 1978. You indicated that is is dropping. My figure is based on physicians receiving National Research Service Awards and I would like to know for the record how you support the idea of declining physicians in research?

Dr. FOX. How do we support it?

The CHAIRMAN. How do you support your assertion that the number of physicians going into research is declining, here, since the National Research Service Awards indicate a level stability with regard to physician research and physicians entering research has remained fairly controlled in recent years?

Dr. FOX. I would have to get you the exact figures on that, sir, and will be happy to submit them for the record. I believe we do have solid figures.

The CHAIRMAN. If you would do that, that would help us. I have been led to believe otherwise, that there has been a level situation; it has not been increasing, but it has not been decreasing either. I would appreciate having this information.

Dr. FOX. Our concern is that we are not recruiting the best candidates and the people whose imagination and initiatives are the ones that we so badly need for this effort.

The CHAIRMAN. Thank you, Dr. Dixon, for your excellent testimony today. As you know, I have strongly resisted attempts to mandate new programs, and to provide line item funding for disease research at NIH. In general, I believe personally that a specification of activities probably is counterproductive. However, as we prepared our biomedical reauthorization bill during the last Congress and gathered information from professionals, patient advocate groups and my staff visited NIH, and so on, I became aware that there was a strong consensus supporting the establishment of a digestive disease centers. Indeed, similar centers conducting research in arthritis and cancer have apparently been productive and cost-effective.

It was the consensus of our committee that these centers be funded, and we conveyed this to NIH last year. However, I have to add, your testimony has been enlightening regarding the apparent failure of the administrators at NIH to act on our recommendations. Consequently, it may be necessary for us to convey a stronger message, maybe even with a legislative mandate. If these centers are established, what, in your opinion, are likely to be the most beneficial results of research in digestive diseases in the future?

Dr. DIXON. First, I share your concern about fragmenting appropriations to an institution such as NIH. I think additional funding with legislative direction would be exceedingly helpful, though, without interfering with the organizational structure, and the IOM study would be of assistance in that. Now, to get on.

I think perhaps one of the most productive areas would be in the diseases of the stomach, as we mentioned, with regard to the prevention of ulcer, understanding the epidemiology of ulcer and things of that sort. I think the second might be in the area of pancreas and in the area of endoscopic procedures, which would take the place of surgical applications. So I think in those three areas, we would see very early results that would be demonstrated both in terms of patient welfare and in terms of economic gain.

The CHAIRMAN. Thank you. I have other questions for you as well. Dr. Engleman, I have a number of questions for you, but I notice we are just getting a rollcall vote. What I would like to do is to provide questions for you to answer in writing, Dr. Engleman, because I am firmly committed to a national arthritis institute. We could use some excellent backup, and any information you submit to this committee will become part of the record.

What I would like to do in the remaining time before I leave to vote is to thank each of you for coming and for the excellent testimony you have given. It has been helpful and enlightening to us on this committee.

I would just call our last witness to the table, and maybe we can finish before I head over to the floor. For our last witness today, I am honored to introduce Dr. Chase Peterson, the vice president for Health Sciences at the University of Utah. Dr. Peterson has recently become a familiar face in households throughout the country as the spokesperson for the university regarding the successful transplant of the artificial heart in Dr. Barney Clark. Dr. Peterson will provide testimony regarding universities throughout the country, representing the Association of American Universities and the Association of American Medical Colleges.

Chase, I could go vote now. It would take me about 10 minutes to go over and get back. Then we could give you more time. Or, I could give you about 6 minutes now, in which you could summarize your testimony. We will put your complete statement in the record, and in that way you will not have to wait.

STATEMENT OF DR. CHASE PETERSON, ON BEHALF OF THE ASSOCIATION OF AMERICAN UNIVERSITIES

Dr. **Peterson**. Thank you, Senator. I will do this in 4 minutes. You have the statement, and it represents the institutes of higher education that do biomedical research and that is the important thing. I can just emphasize three things.

One is that this is my first hearing in Washington. Before I become jaded, let me congratulate you and Dr. Sundwall and his associates. The alternative to what you are doing here is simply to rely on power politics and backroom politics. I, for one, greatly appreciate and am impressed by the process that has been gone through, where these gentlemen have been able to put their things on the record, you are going to sift them, your staff is going to sift them and come out with good policy. That is democracy, and I am very grateful for part of it.

The **Chairman**. I agree with you.

Dr. **Peterson**. The second thing I want to say is that our institutions say that NIH works well. At a time when welfare does not work very well, and law enforcement does not work very well, and innercity schools do not work at all, NIH works and is doing a darned good job. We appreciate your approach to it, which is to monitor it, to oversee it in a tough fashion but to let them manage it. That has been very useful.

The third thing is something I have not heard today, and maybe it will be useful. Your bill has our full support. Your willingness to increase funding 10 percent last year and 5 percent this year keeps those constant dollars supporting it. You will have opponents that will want to cut that. The administration wants to give less. Maybe one simple idea might be of value to you and your staff as you face that onslaught to cut it.

Money that goes into biomedical research has given us all in America and the world a better way of life and better health, and for that we are grateful. That is enough to justify it. But at the same time, now we are facing a cutback in Federal expenditures. We do not have enough money to do all the good things that we would like to do. Part of health research helps us live a better life, sure, but to have a better life you also had better not outlive your savings. You had better not have inflation ruin your savings. That is a medical disease, to my way of thinking. If you do not have a job, that is a medical disease. So you and others have taken the lead in trimming the Federal budget as a way to get back to jobs for people and a way to control inflation.

I would like to suggest that this is part of biomedical funding, but we should be willing to take cuts. We have taken cuts, but biomedical research helps us to a better life. We want symphonies, we want libraries, we want good health. All that has to be cut a bit, but there is a second part to biomedical research and that is the contribution it makes to productivity, and I mean industrial productivity.

Daniel Bell, the man who coined the phrase "postindustrial society," has commented that America can only really exceed the rest of the world in productivity in two areas, our soil and our basic research. We cannot make new soil, but we can make new basic research. When Einstein did photoelectric cells, when we have had quantum mechanics, those are the things that allowed us to stay competitive in this country. It is very clear, Nobel prizes have not been given to Japanese. That is not a racial statement because many people of Japanese extraction have done work in this country and received Nobel prizes. But the Nobel prizes have come to this country and western Europe. That is our advantage.

I would just, in this last minute, suggest that while the comforts of life which are represented by biomedical research ought to share in the cuts, as should the symphonies and the libraries, the other part of biomedical research, which is contributing to our edge in productivity in this country—I am talking about genetics, about polymers, about plastics—these are the things that allow us to be productive in this world. If we do not do that, we will be as foolhardy as Chrysler Corp. would be to cut back on R&D at a time when they fear the market competition. They have been smart enough to abandon their policy of the 1970's, which was to cut back on R&D, and to get back into research and do it right. Maybe they will succeed.

I am hopeful that your appropriation suggestion will hold. If it were to go even higher, that would be fine, but I know the pressures on you. But I am saying, we are grateful for that. It does two things: the quality of life, but also American productivity. That is enough to say right now, Senator.

[The prepared statement of Dr. Peterson follows:]

PREPARED STATEMENT OF DR. CHASE PETERSON

Mr. Chairman, and members of the Committee, I am Dr. Chase Peterson, Vice President for Health Sciences at the University of Utah. I speak to you in behalf of the Joint Committee on Health Policy of the Association of American Universities, the American Council on Education, and the National Association of State Universities and Land-Grant Colleges. In as much as the institutions of higher education comprising the memberships of these organizations conduct the vast preponderance of biomedical research in the United States, and since the major portion of financial support for that research comes through grants from the National Institutes of Health, that we are, understandably, concerned with legislation before your committee that would affect the future operations, structure, and policies of NIH.

Basic courtesy and longstanding practice usually calls for witnesses before committees like this to commend the members of the committee for their support of programs on which the witness is testifying. I wish that such custom and practice did not exist, so that no one could assume a formulistic or ritualistic comment in my next statement. The stature of American biomedical science probably could not have been imagined a few decades ago. The exciting and wonderous advances made in discoveries of the causes of disease and the means for preventing or alleviating and more frequently curing those diseases, would not have been predicted by the most optimistic Pollyanna even a few decades ago.

Popular publications sometimes give us the best clues to how we are thinking about fundamental issues. This month's Readers Digest has a wrap-around cover that proclaims in extra large type "Closing In On Cancer." Obviously, simplistic. Possibly not statistically or scientificly accurate. Not even beginning to hint at the complexity of the challenges still before biomedical research before that headline is a reality. Nevertheless, it is a highly imaginable statement. It no longer is out of the question that in the lifetime of many, if not most of us sitting in this Congressional hearing room, it will be possible for physicians to prevent or cure a very substantial number of the various forms of malignancies that plague humankind today.

Too few of our citizens understand now, or probably will understand in the future, how this dedicated campaign against disease came to reach its exciting zenith in this country in the past two decades, and who were responsible for that happening. Not enough will understand how national health policy is formed in rooms like this, in the offices of the leadership of the Congress who choose to fulfill our democracy's promise to its citizens,to enhance their fundamental wellbeing and protect them from unnecessary pain, suffering, and tragedies accompanying disease and death.

Some of you have been part of this campaign for a good long time, and others have taken up the responsibility only in the past two years. But all of you have combined in remarkably limiting political differences to create, support and advance biomedical research through the remarkable institution known as the National Institutes of Health. You have followed your role on an authorization committee to encourage your colleagues on budget and appropriation committees to realize the possibilities of the law for adequate funding. You have acted to protect NIH or specific programs under its aegis from occasional maladroit attempts that would adversely affect its operations, and other times from well meaning, but public servants who have difficulty understanding what is meant by the spirit of the law. Mr. Chairman, just in the 97th Congress you asserted your leadership role in a number of ways that helped protect the National Research Service Award programs exemption, that helped deflect a illconceived notion by HHS officials to unilaterally reduce reimbursements for indirect costs to institutions, and, most significant, your stand on the place of NIH research to encouraged your colleagues to support funding for the NIH that stemmed a period of decline begun in 1980.

Mr. Chairman and members of the Committee, given your past admirable performance in support of biomedical research, it is not surprising that it is reflected in the bill before us today, a bill that we are pleased to lend our support to as you move forward in the legislative process. We say this is a good bill because it recognizes the valuable nature of NIH. It shows a comprehension of how the institutes evolved over time in their own peculiar ways, probably illogical at times to textbook management, but successful nonetheless in achieving fundamental scientific objectives. Perhaps most important, the bill contains in it a basic endorsement of NIH's purpose, the support of the individual investigator conducting biomedical research.

We have to admit that Title IV of the Public Health Service Act is rather messy. It may be no way to run anything, let alone an extraordinary $4 billion annually funded research enterprise. But we serve the nation ill if we tinker with something that has stood the repeated tests of time as the proper legislative background or matrix for the National Institutes of Health.

Where we find ourselves at the moment with regard to NIH might best be summarized by an anecdote by of an event that took place in New York City's Lincoln Center just after it opened, about two decades ago. While the Center was still spanking new, and resplendent with its brocades and velvets and other beautiful decor, there came for a one evening performance Victor Borge, the Danish pianist/comedian. To a packed audience he strolled out from backstage carrying a hand microphone, trailing electrical cord. He began his somewhat zany patter at once, and with the audience already engrossed in laughter, he announced that he was going to speak to the people in the audience, and strolled toward them. When he was still some 20 feet away from the edge of the stage he found that the microphone would not move further. He tugged a few times and then realized he had run out of microphone cord. He gazed slowly at the gorgeous decorations in the concert hall, and then sadly noted:

"Just think. For eighty-nine cents more we could have gone all the way."

Mr. Chairman, as we have noted earlier, the support for NIH in the past two decades has been strong, and has built it into the magnificent research institution it is. But charts that show funding for NIH in constant dollars, note extraordinary support in the 1960's, still growing supporting in the 1970's, peaking in 1979. In 1980, 81, and 82,the charts show real declines of about 5% each year. Action by the Congress last year in the Continuing Resolution reversed that trend so that the decline seems stemmed. However, were the Congress to accept the Administration's funding proposals for FY'84 we would experience once again a cutback in real funding, manifested by a serious decline in the number of awards, in the size of awards, in support for training and the other mechanisms that comprise the NIH programs.

We are quite aware, as administrators in the nation's universities and medical centers, of the impact the economy has had on state budgets, and through them on public universities, and, occasionally on private university funding. We are very conscious as citizens of this country of the problem of annual deficits, and we are aware that Congress must balance many claims to available funds.

If one speaks to research directors in almost any scientific discipline and asks what is needed, honest answers will frequently start with the word "more," but the most important word following that one is "stability." The finest biomedical research scientists in this country would be willing to invest more of their careers, their time, their energies. The institutions to which they belong would feel justified to commit more of their own funds, and space and personnel. Where the private sector enters into this arena, it too, would be prepared to take more risks with the assurance that what was begun in 1983 would be supported at no less a level in 1988 or beyond.

One of the reasons for the great chapters in NIH's history so far may be attributed to those years when the scientist could assume that they could embark on projects and see them through, and even develop them further because adequate funding would be available. We recognize that before us today is an authorization bill, not an appropriation. Still, we wish to take this opportunity not only to thank you for what you have done in the past, but to urge you on to continue your supportive role in seeing that what you authorize does in fact carry through.

I will use this opportunity to set forth five central points that represent our association's concerns and recommendations regarding the immediate future of the National Institutes of Health. Before I do that, I feel obliged to create a parenthesis in my testimony to express special thanks to the Chairman and members of the Committee for the manner in which they have responded to proposals that would reduce reimbursements to institutions that come under the general heading of "indirect costs."

Had we had the forsight to invisage current times and current fiscal pressures on agency administrators, we might have been more judicious in our nomanclature. As you know, like almost all of our endeavors, the conduct of research costs money. It costs money to pay salaries for senior scientists as well as laboratory technicians. It costs money to purchase and maintain instruments and to pay for supplies used in the conduct of experiments and tests. It costs money to heat and air condition laboratories, to maintain libraries in which research is conducted on biomedical matters relating to work simultaneously occurring in laboratories. It also costs money for administrators to handle the many transactions related to the conduct of research.

All of these are necessary, proper and justifiable expenditures. They have only one difference among them; some can be precisely measured and assigned to a particular project; others can be measured in terms of an entire research enterprise, but would prove wasteful to determine precisely how much belonged to any one grant. Thus, the terms direct and indirect costs. It borders very closely on deception for any federal agency administrator to speak of "research costs and indirect costs."

There is nothing arbitrary about the level of indirect costs assigned by the federal government to an academic medical center. These are determined over long periods of time through negotiations among highly skilled accountants in both the government and the university community. All expenditures are audited by federal auditors. Every grant awarded at NIH, prior to the award, has had a cost evaluation made by the study section that evaluated the substance. The recommended level of the study section is subject to further evaluation and negotiation with the principal investigator by the business officers of NIH. It may a long tortuous process, but it is designed to assure that the American citizen, through his government, is getting what he pays for and that recipients of federal support are wholly accountable for the use of federal dollars.

But the system is very complex and not too many people can claim a mastery over the accounting intricacies involved. It is an ideal subject area for officials cornered by inadequate funds to play mountbank, playing to the unhappiness of harried officials and members of the research professions themselves who do not wish to see cutbacks in the support of the conduct of research.

There is a set of principles represented by OMB Circular A-21 that also took a very long period of time to carve out as the standards to which all parties would adhere. The university community representatives might have thought twice before participating in that long negotiating process if they had been told that A-21 would become a set of strictures to which they would be bound, but which government agencies would be able to deal with arbitarily. We respectfully submit that this Committee consider making any standard dealing with the determination of appopriating direct and indirect costs, one that binds both parties - the university and the federal agency.

You will recall that last year NIH proposed cutting indirect costs by ten percent. There was no particular reason for that percentage rather than another, no suggestion that it was that percent by which indirect costs were "overcharged." There was instead an allagation that indirect costs had been skyrocketing and threatened to devour funds for direct costs. (Again, a seperation of the two types of costs which are inseperable in the conduct of research.) The Chairman and many members of this Committee were vocal in their opposition to such capricious behavior. Your views influenced your colleagues in the appropriations committees who funded NIH for FY'83 at an adequate level to reimburse the institutions at the agreed upon level for the cost of research.

The draft justifications sent to the Congress in late January from NIH repeat the regrettable approach of last year towards indirect costs, this time, not speaking in terms of percentages, but sighting of figure of $72 million. At the direction of the Congress, in the Continuing Resolution for FY'83, officials of HHS, four weeks ago, convened a meeting of representatives from the university community. I regret to say that despite more than two hours of discussion, there was no meeting of the minds since we continued to find it impossible to begin a discussion that requires the agreement to assumptions that have no basis in fact. Our discussions have been cordial and we have complied with the request that we include our views with the report that HHS must send to the appropriation committees prior to their testimony on the FY'84 budget during this month.

We believe our position to be reasonable. Universities always have been engaged in cost sharing, and the government generally does not pay full cost of research. Because of fiscal constraints NIH undertook, during the past year, to trim grants by 4-8% generally, though in some instances the cuts in direct costs were as high as 20%. These cuts were not in nonessentials. NIH did not suggest that somehow, someone would have to pay for these costs. Indeed, our universities are absorbing a larger cost sharing responsibility because of this continuing practice at the NIH. Our call is for equity. There is a complex mechanism in place that determines costs, there is a set of principles established to help determine what the costs are and how they shall be met. If a request for funds is unjustified, it should be denied. If it is justified, it should be paid according to established principles. We hope that this committee will continue to support the universities position so that it may be resolved equitably.

One point we would stress is that although it is seen as a mission agency created and supported for the purpose of preventing and curing disease, the National Institutes of Health is generally engaged in supporting basic research. Much of its success has been rooted in its freedom to identify opportunies wherever they grow in scientific disciplines, to attract the best people who have the finest ideas and to be able to follow with funding these ideas and these opportunities. As noted above, when NIH was genuinely growing it could fulfill these aims. This has become increasingly difficult as funds have decreased.

One important test of the decrease is in the "paylines" the levels at which proposals have been funded. (Scores at NIH are in reverse order: the lower the score, the more highly rated the proposal.) During the 1970's it was common for proposals receiving scores between 250-300 to receive funding. Currently the awards are not going much beyond scores of 180. There is little question but that high quality science is contained in proposals with scores of 200-250 that are going unfunded.

We fear that many of these proposals are from young faculty who have not yet quite made their mark as research scientists, who will be denied the opportunity for doing so. We noted earlier the overriding importance of stability; we need to stress that this stability calls for adequate funding of research grants and not partial and cutback funding of grants that require changing scope and approach of research programs. Also noteworthy is that while stability is vital there is no magic number.

Some years ago, the figure 5,000 appeared as a target for a minimum number of awards annually in the new and competing category. Based on previous experience, the number is a reasonable one, but not if it results in virtually every other mechanism at NIH being cut back - training, centers, clinical trials, as well as parts of grants - in order to achieve this aim. Nor is the number meaningful if it is a ballooned sum resulting from percentages of grants stolen from 4,200 other grants, for example, to create 800 more that are also truncated. We join the associations of scientists in their concern that too few grants will reduce faculty and injure the enterprise as a whole, and we join them in a campaign to convince the Congress of the need to provide funds sufficient for NIH to make adequate numbers of fully funded grants annually.

A second concern lies in the area of training. The number of awards at NIH has dropped considerably in recent years. More important, we are not training an adequate number of M.D./Ph.D. scientists who can bring their specialized skills to bear on the research process. It may be necessary to study carefully the incentives needed to attract and keep in research these physicians who might be lured away by the more lucrative practices. The debt accumulated in obtaining an M.D. degree might be such a factor, and how we deal with it to neutralize its affect may be significant.

We commend the Chairman directly for dealing with a noisome problem - the IRS' insistent claim that National Research Service Awards are taxable as a result of a payback provision in the law. Your repeal of the payback provision should remove the fundamental argument of the existence of a quid pro quo in the award and should make it easier for IRS to accept the award as a nontaxable scholarship.

Our third area of special interest is young façulty. For many complex reasons this nation has entered a period of serious crisis in engineering educaton. There are 2,000 faculty positions for which funds are available that cannot be filled. Too few engineers are being trained in our nation's institutions today because of the shortage of faculty and the implications for business and industry are obvious.

We do not suggest direct parallels between tha field and biomedical research. Such parallels rarely exist between diciplines, but principles may be learned from one part of the university to another. We must deal with the situation at hand rather than one more comfortable. Sixty years ago, the circumstances in biomedical research were such that the perpetuation of the enterprise could be counted on through a natural process of attracting fine minds dedicated to science. The enterprise, however, has grown wonderfully. If we are to maintain our place on the world as the outstanding center for biomedical research, if we are to continue to maintain the great centers of medical research on our campuses and independent centers, it is imperative that we be able to attract the best people into the academy and make opportunities available to them that has them find on academic research career most attractive. NIH sustains a modest program, but it does not confront the challenge directly. We believe this area deserves increasing attention by the Congress of the United States.

A fourth concern is one that has been receiving increasing attention in the physical sciences and is manifested positively in the FY 1984 budget - that the problem of instrumentation and equipment. The 1979 study conducted by AAU in conjuction with the NSF showed instruments in university laboratories were generally twice as old as comparable instrumentation in industry. While that study focused primarily on the physical sciences, where it touched on biomedical research, its findings were not contradictory. Were NIH to undertake an in depth study of the problem, it would be able to provide in depth analysis and descriptions of this sorry situation. We believe that such studies may not be necessary to assert that considerably more support is desperately needed for instrumentation and equipment if our scientists are to be able to conduct research at the frontiers of their diciplines.

This ties closely to our final concern - research facilities. It has been a considerable time since NIH had the wherewithall to assist institutions in building or renovating structures used for the conduct of biomedical research. Some extraordinary construction was accomplished. But, unfortunately, buildings wear down and after two decades considerable funds are needed to bring them back into the condition that enabled them to play the role for which they were created. There is a wide array of construction involved, ranging from buildings to house research animals to clinical hospitals. But these structures and the instruments within them are essential in maintaining a research base for our scientists to operate in.

We recognize that this is a long term problem with a long term solution that will not respond to one emergency "shot in the arm." We suggest that this Committee, which has done so much to build the biomedical research base of the nation must look into ways in which to renovate it and refurbish it and at times rebuild it. It must recognize that it will take funds and that they will not be able to be appropriated unless adequate authorization levels are established by the Congress.

Mr. Chairman and members of the Committee, as you know, at my institution, the University of Utah, in recent weeks, we have been involved in an aspect of biomedical research activity that has been both astounding and energizing. It has been my responsibility to brief the press and other media representatives on the progress of our aritificial heart patient. The unusual and exciting nature of the surgery and treatment of Dr. Clark warranted the news coverage over so long a period of time. I wish that circumstances were such that the media were to give similar and constant attention to all that went in to enabling the work at the University of Utah to take place.

I would like to see the popular press devoting much space to describing the painstaking work of the thousands of men and women over decades of time in developing knowledge that led to further knowledge that led new antibiotics, anasthesias, analgesics. I would like to see described in appropriate detail the surgery conducted an animals to test again and again until a procedure or instrument or tool was sufficiently reliable to use it on a human being. I think that if the American public could understand all that is accomplished by the idea of biomedical research, the task you are doing so well in seeking to enhance that work would be much easier and that unlike Mr. Borges microphone cord, creative ventures into biomedical research would not run out because of a shortfall of a comparatively few dollars.

Our democracy thrives when its government and most talented people enter into a partnership in behalf of the welfare of all. You have played your role admirably and we are grateful for it. I will be pleased to answer your questions. Thank you.

The **Chairman**. Thank you, Chase. We appreciate your excellent statements, both oral and written, that you have provided for the committee. I just want to personally thank you for all the help you have given me through the years, and especially during the last 2 years when I became chairman of this committee as a 4-year freshman Senator. It is a committee with far-reaching jurisdiction, overseeing approximately 3,000 various statutes, 260 entities of government, and three Cabinet-level departments. No other committee has that kind of wide-ranging reauthorization jurisdiction. It has been very challenging for me, and you have been one of my tremendous resources as I serve here. I just want you to personally know that.

Dr. **Peterson**. I appreciate that. When you want to choose a new illness to have, let me give you some advice. There are better ones than Achilles tendons.

The **Chairman**. You are telling me.

I surely appreciate your being here. With that, we will recess this committee at this time and, we are hopeful, mark up this bill within the next few weeks.

[Additional material supplied for the record follows:]

aamc association of american medical colleges

JOHN A. D. COOPER, M.D., PH.D.
PRESIDENT

202: 828-0460

March 30, 1983

The Honorable Orrin G. Hatch
Chairman
Committee on Labor & Human Resources
United States Senate
Washington, D.C. 20510

Dear Mr. Chairman:

The Association of American Medical Colleges (AAMC) is pleased to have this opportunity to submit for the record its views on S.771, "The Biomedical Research, Training and Medical Library Assistance Amendments of 1983," legislation to renew the authorities for several vitally important research programs of the National Institutes of Health. Its significance to the Association, which serves as the national representative for the academic medical centers, is based on the fact that about half of all NIH supported biomedical and behavioral research is performed in these institutions.

As members of this Committee are well aware, this represents the third time in recent years that the Congress has embarked upon the renewal of these programs. The previous two Congresses were unable to reach a consensus on a final proposal.[1] Thus, this third effort seems to provide the appropriate occasion to reflect on the nature of biomedical and behavioral research, what promise this process holds for the future and what is necessary for it to continue to flourish.

The past few decades have been an unbelievably exciting era of scientific progress, characterized by the outpouring of an ever increasing number of new discoveries. The sense of expectancy that permeates biomedical science today can be accounted for primarily by the widespread recognition of expanding opportunities for progress in science and in the conquest of disease. Scientists in virtually every field of biomedicine now perceive new points of attack, fresh

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[1] While one renewal statute, P.L. 96-538, was enacted in the 96th Congress, it was for only a two-year period and did not reflect the contents of the bills introduced and debated---S.988 and H.R.7036.

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approaches and promising leads to hitherto intractable problems. This state of affairs is in large measure the consequence of a partnership that has flourished for the past forty years between institutions of higher education and the Federal Government. Together they have succeeded in developing a superb infrastructure for the exploitation of scientific discovery aimed at the amelioration, diagnosis, cure and treatment of disease.

NIH STATUTORY AUTHORITY

Central to this success has been the administrative and legal structure for the National Institutes of Health---the permanent and broad-based research authority set forth in Section 301 of the Public Health Service Act, carefully crafted to ideally match the processes under which science is characteristically coducted. Section 301, the continuing legislative underpinning of the NIH and its components provides exemplary but not exhaustive or limiting specifications of how this authority is to be exercised. The Congress very wisely---in our estimation---saw fit to establish NIH with a statutory base admirably designed to exploit to the maximum this nation's investments in research, a base that facilitates the rapid but careful redirection of scientific effort and funding flows to exploit new discovery. Under this authority, administrators of the NIH have had the freedom and flexibility to react both promptly and effectively to exploit opportunities that, almost as the rule, emerge suddenly and unexpectedly and to sustain continuously a broad-base of excellent research. Decisions on where and how to most effectively funnel Federal dollars, as determined by a consensus of the most eminent scientists, have been encouraged and science administrators have been allowed the freedom to follow such advice.

This broad-based statutory authority, first enacted by the Congress in 1944, remained virtually untouched until 1971. The enormous success of the National Institutes of Health during that period is ample testimony to the wisdom of this authority: it permitted full reign of the creative genius in administration of research programs that has made the NIH great.

RECENT LEGISLATIVE HISTORY OF THE NIH

The Association is convinced that the modifications made to the NIH's statutory base in 1971, by terminating the permanent open-ended authority under which the National Cancer Institute traditionally operated and under which the other institutes (except NHLBI) continue to operate, has had serious and unforeseen ramifications. At that time, Senator Gaylord Nelson warned that this was:

> "...the first giant step in the dismantling of the NIH"..."The National Heart and Lung Institute has now requested that they be treated in the same fashion...Their case will be just as good as a case for a separate cancer institute..."

Regrettably, Senator Nelson's latter prediction was realized within the year with the enactment of P.L. 92-423 authorizing the creation of a separate National Heart and Lung Institute; moreover, the Association is becoming increasingly concerned that the proposals advanced in the past thirteen years---particularly those of more recent vintage---are lending more and more credence to his former insight.

Since passage of the National Cancer Act, a host of narrow interest groups have sought "quick fixes" and "legislative solutions" for their putatively unique needs and problems. To illustrate this point, appended for the record is a chronology of the 20 statutes enacted in the past thirteen years, directing the NIH into ever more narrowly defined categories and activities. Apprehension concerning the potential cumulative impact of this gradual but inexorable erosion of the flexibility so vital to the continued productivity of the scientific enterprise has been articulated throughout the years by members of the Administration and the Congress from both parties:

- "...no mere change in organizational form will cause a research area to flourish..." Elliot R. Richardson, Secretary of the Department of Health, Education and Welfare concerning "The National Institutes of Arthritis, Metabolism, and Digestive Diseases Act" (P.L. 92-305).

- "The series of special disease bills which we have been writing represents an approach to the problems of the NIH comparable to trying to save the ship Titanic's problems by repairing the lifeboats when the ship itself could be saved." Representative John Dingell (D-MI) concerning "The National Cancer Act Amendments of 1974" (P.L. 93-352).

- "...I do not believe that we are going to improve the management of scientific research by creating an evergrowing panoply of official lobby groups for each disease..." Senator Thomas F. Eagleton (D-MO) on "The Arthritis, Diabetes and Digestive Disease Amendments of 1976" (P.L. 94-562).

- "As the National Institutes of Health have grown and expanded their activities, multiple special interest groups have surfaced to vie for enhanced support for specific disease related research... I am firmly convinced that the research process works best and is most likely to be productive, when it is unfettered by multiple legislative mandates and constraints...attempts by legislators, in response to well-intentioned special interest groups, may hamper instead of help the overall research effort." Senator Orrin G. Hatch (R-UT) concerning introduction of S.771, "The Biomedical Research, Training and Medical Library Assistance Amendments of 1983."

CURRENT LEGISLATION

This situation has reached the point where, today, extremely hard choices face the members of this Committee. The Congress, and most particularly this Committee and its counterpart panel in the House, have been inundated by a plethora of requests to establish in statute new institutes, program "earmarks", separate authorizations, novel committees, studies, commissions and so forth, directed at a growing list of highly specific disorders and diseases, for each of which almost invariably a cogent case can be mustered, by citing the impact of the disease in question on the nation as a whole and by cataloguing the aggregate national pain and suffering that it inflicts on our citizens. The Association is particularly concerned by the response given to a host of such requests that have been included in the counterpart legislation on the House side, H.R. 1555, "The Health Research Extension Act of 1983." In addition, to carry out the inescapable imperative of the moment---the renewal of various expiring authorities---H.R. 1555 provides for:

- A $1 million set-aside and a $4 million authorization to establish and carry out the activities of a National Commission on Orphan Diseases.

- A separate authorization for mental retardation at the levels of $8, $9 and $10 million for the next three fiscal years.

- A $4 million set-aside of NIH appropriations for the next three fiscal years to carry out the functions of the National Center for Health Care Technology (NCHCT).

- The establishment of a separate line authorization for the cancer research and demonstration centers, currently funded under NCI's aggregate appropriation.

- A separate authorization for basic and clinical research on spinal cord regeneration, with spending ceilings of $21, $24 and $27 million for FY 1984-86.
- The establishment of a program of Centers for Research and Demonstration of Health Promotion and Disease Prevention, with authorization ceilings of $10, and $20 and $25 million for FY 1984-86.
- The authority for establishment of a separate arthritis and musculoskeletal disease institute.
- The transfer of the National Center for Health Services Research (NCHSR) to the NIH.
- The transfer of the National Center for Health Statistics (NCHS) to the NIH.
- The transfer of the National Institutes on Occupational Health and Safety (NIOSH) to the NIH.
- The establishment, for the NIH and for each individual institute, of positions for an Assistant Director for Prevention, to administer and promote such research programs within each of the institutes.
- A requirement for a "prevention plan" for NIH supported research.
- The establishment of an interagency committee on spinal cord regeneration research.
- The establishment of a new subcommittee for the statutorily mandated Interagency Technical Committee on Heart, Blood Vessel, Lung and Blood Disease and Resources to focus on lung research.
- The establishment of an interagency committee on learning disabilities.
- A study of the role of diet therapy in the treatment of end stage renal disease.
- A study on the safety and effectiveness of the pertussis vaccine.
- A study of the adequacy and availability of personnel to meet the health care needs of the elderly through the year 2020.

- A study to examine the questions surrounding the commercialization of biomedical research.
- Restrictions on fetal research.
- A separate authorization for "alternative methods" research.
- A requirement for a research plan for "alternative methods".
- A mandate for the promulgation of regulations for animal care and treatment and the establishment of animal care committees.
- A "budget by-pass" for all of the NIH.

Specifications of this order of detail are not the only ones included in the renewal of the NIH authorities; the House version also contains directives concerning the management of the NIH. In toto, these constitute a cumulative list of proposals that have been advanced since the Congress began trying to renew the NIH authorities in 1979. Unfortunately, every year the length of the list grows.

While enactment of one or even several of these would not fulfill Senator Nelson's dire prediction for the research enterprise, the culmination of a few years of this type of legislation certainly would. Given these circumstances, the Association is quite frankly fearful for what the future may hold. The most recent spate of proposals has raised the troublesome spectre of the explosive fragmentation of the National Institutes of Health, a national symbol of excellence, into a congeries of administratively top heavy programs that will spend scarce dollars chasing will-o-the wisps, while good science will be left unfunded.

As this Committee well knows, it has become extremely difficult to fill the senior posts at the NIH---as elsewhere in the Government ---due to the inability to compete with private sector salaries. Fortunately, the opportunity to administer an institution of such excellence has been an overriding factor and the NIH has always been able to recruit the best and the brightest. However, the additional constraints imposed by legislation of this genre will only serve to make positions more unattractive and may well deter even the most dedicated.

RECOMMENDATIONS

As you are well aware, the National Institutes of Health has become deeply concerned about the viability of its present organizational structure and has requested the National Academy of Sciences (NAS) to embark upon a comprehensive review of this matter. Therefore, the Association strongly urges that only the simplest of renewals be enacted, pending the results of this study. Moreover, the Association would urge the Committee to exercise detailed oversight over the agency through a carefully crafted hearing process. This would permit the Committee to concentrate on the many complex and knotty problems of administration, accountability, ethics, and research emphases that are usually not most effectively solved by legislation.

The Association appreciates this opportunity to discuss its concerns with the members of this Committee and is deeply appreciative of its support of the research enterprise. We stand ready to assist the Committee in any way with the development of this legislation.

Sincerely,

John A. D. Cooper

John A. D. Cooper, M.D.

cc: Members of the Senate Committee on
Labor and Human Resources

Appendix I

Legislation Affecting the National Institutes of Health Enacted Subsequent to "The National Cancer Act of 1971"

December 23, 1971	P.L. 92-218. "The National Cancer Act of 1971" established: The National Cancer Institute with time and dollar limits; the National Cancer Advisory Board; a separate authorization for cancer control centers; the President's Cancer Panel to monitor the cancer research program; a "budget-bypass" for NCI; and a requirement that the NCI and NIH directors be appointed by the President.
May 16, 1972	P.L. 92-294. "The National Sickle Cell Anemia Control Act" established a national program and separate authority for diagnosis, treatment and research into sickle cell anemia.
May 19, 1972	P.L. 92-305. Renamed the National Institute on Arthritis and Metabolic Diseases as the National Institute on Arthritis, Metabolism and Digestive Diseases and established: the post of associate director for digestive diseases; and a digestive disease subcommittee within the Advisory Council.
August 29, 1982	P.L. 92-414. "The National Cooley's Anemia Control Act." Authorized funding for research into the diagnosis, treatment and prevention of Cooley's anemia and for counseling and public information programs.
September 19, 1972	P.L. 92-423. "The National Heart, Blood Vessel, Lung and Blood Act" established: time and dollar limits on the Heart and Lung Institute; a separate authorization for prevention and control programs; and a National Heart and Lung Advisory Council.
October 23, 1972	P.L. 92-563. "The National Commission on Multiple Sclerosis Act" established a National Commission to determine the most effective method of finding a cure for multiple sclerosis and to make specific recommendations for maximum utilization of national resources directed toward this research.
April 22, 1974	P.L. 93-270. "The Sudden Infant Death Syndrome Act of 1974" authorized specific and general research in this area through the National Institute of Child Health and Human Development and provided an authorization for data collection and counseling programs.

May 31, 1974	P.L. 93-296. "The Research Aging Act of 1974" established: a new National Institute on Aging; a national advisory council; and a requirement for a research plan.
July 12, 1974	P.L. 93-349. "The National Research Service Award Act of 1974" repealed longstanding research training authorities in the PHS Act and substituted therefor a new program of individual and institutional NRSAs with pay back requirements. It also created the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, mandated that grantee institutions establish Institutional Review Boards and limited research on the living human fetus.
July 23, 1974	P.L. 93-352. "The National Cancer Act Amendments of 1974" provided for: the renewal of the NCI's authority; the consent of the Senate for appointment of the NIH Director; peer review of NIH and ADAMHA grant applications and contract projects; and the establishment of a President's Biomedical Research Panel to review and make recommendations concerning NIH and NIMH research programs.
July 23, 1974	P.L. 93-354. "The National Diabetes Mellitus Research and Education Act" established: a separate authorization for the establishment of centers for diabetes research and training; a National Commission on Diabetes to formulate a long range plan to fight diabetes; a Diabetes Mellitus Interagency Coordinating Committee; and a post for an associate director for diabetes within the National Institute for Arthritis, Metabolic and Digestive Diseases.
January 4, 1975	P.L. 93-640. "The National Arthritis Act" authorized: the establishment of a National Task Force on Arthritis to develop an Arthritis Research Plan"; an earmark of at least $500,000 of NIH appropriated funds for orthopedic research dealing with arthritis; the establishment of a separate authorization for arthritis prevention and control programs; the establishment of a separate authorization for arthritis research and demonstration centers; a position for an associate director for an associate director for arthritis; the creation of an Inter-Institute Arthritis Coordinating Committee, an Intradepartmental Arthritis Coordinating Committee, an Interagency Technical Coordinating Committee on Arthritis; and the submission of an annual report to the Congress with a "Five Year" plan for arthritis.

July 29, 1975	P.L. 94-63. "The Special Health Revenue Sharing Act of 1975" created two special interest Commissions, one "For the Control of Epilepsy", the other "For the Control of Huntington's Disease".
April 22, 1976	P.L. 94-278. "The Health Research and Health Service Amendments of 1976": extended authority for the National Heart and Lung Institute for one year; renamed the Institute as the National Heart, Lung and Blood Institute; specified increased emphasis on blood-related research; authorized the establishment of ten blood centers; and required the Secretary of HHS to give priority to applications for research grants and contracts on Sickle Cell and Cooley's anemia.
October 19, 1976	P.L. 94-562. "The Arthritis, Diabetes and Digestive Disease Amendments of 1976" provided for: the extension of the diabetes and arthritis research and training programs; the establishment of a National Arthritis Advisory Board and a National Diabetes Board; and created a National Commission on Digestive Diseases to develop a long range plan for digestive diseases research.
August 1, 1977	P.L. 95-83. "The Health Planning and Health Services Research and Statistics Extension, Biomedical Research and Extension, and Health Services Extension Act" provided for a one-year extension of the programs of NCI and NHLBI.
November 6, 1978	P.L. 95-602. "Rehabilitation Comprehensive Services, and Developmental Disabilities Amendments of 1978" mandated coordination of NIH and its programs with those of the newly established National Institure of Handicapped Research.
November 9, 1978	P.L. 95-622. "The Biomedical Research and Research Training Amendments of 1978": provided for a two-year extension of NCI and NHLBI; mandated that NHLBI disseminate information on nutrition and environmental pollutants; and required that both NCI and NHLBI's research and demonstration centers provide for continuing education of health professionals and conduct public information programs. It revised the membership requirements for the NCI Advisory Board to include non-voting representatives from other Federal agencies and to include individuals knowledgeable in environmental carcinogenesis. In addition, P.L. 95-622 required the Secretary to: conduct studies and tests of substances for carcinogenicity and other harmful

	effects; establish and conduct a comprehensive research program on the biological effects of low-level radiation; conduct and support research on human nutrition; and publish an annual list of known or suspected carcinogens.
December 12, 1979	P.L. 96-142. "The Emergency Medical Services Systems Amendments and Sudden Infant Death Syndrome Amendments of 1979" requires NICHD to assure that its appropriated dollars are used for research into the cause of SIDS and to provide the Congress a detailed report on activities in this area.
December 17, 1980	P.L. 96-538. "The Health Programs Extension Act of 1980" provided a two-year extension of NCI and NHLBI when the House and Senate were unable to reach agreement on two measures which would have significantly altered NIH's statutory authority. In addition, P.L. 96-538: redesignated the National Institute of Arthritis, Metabolism, and Digestive Diseases as the "National Institute of Arthritis, Diabetes, and Digestive and Kidney Diseases; established Advisory Council subcommittees for arthritis, diabetes and kidney diseases; created the position of Associate Director for Kidney, Urologic and Hematoligic Diseases; and established a Diabetes Data System and a Digestive Disease Advisory Board.

STATEMENT OF

THE AMERICAN COLLEGE OF CHEST PHYSICIANS

presented by

W. Gerald Rainer, M.D.

regarding
S. 773 -- The Biomedical Research Training
and Medical Library Assistance
Amendments of 1983

Submitted to
Committee on Labor and Human Resources
Senator Orrin G. Hatch, Chairman

Mr. Chairman and Members of the Subcommittee:

My name is Dr. Gerald Rainer, Clinical Professor of Surgery, University of Colorado Health Science Center. I am also the President of the American College of Chest Physicians, a professional medical specialty society of more than 11,000 physicians, scientists, and educators who specialize in diseases of the heart, lungs, and circulatory system. It is in this latter capacity that I submit this testimony on S. 773.

I would like to take this opportunity to express our gratitude for your having afforded us the opportunity to submit our views on legislation which would extend the legal operating authorities of the National Heart, Lung and Blood Institute, and the National Research Service Awards Program as well as other significant amendments in the programs of the National Institutes of Health. We appreciate this early effort on your part in introducing S. 773, "The Biomedical Research, Training, and Medical Library Assistance Amendments of 1983." We hope that the introduction of this legislation and the expeditious scheduling of hearings will assure that the legal operating authorities of the National Heart, Long, and Blood Institute will be extended at sufficiently high authorization levels.

For more than fifty years, heart and blood vessel diseases have been major causes of death in this country, accounting for over fifty percent of all deaths annually. They represent more than twice the number of deaths from cancer, the next highest cause.

Lung diseases, themselves, have become a very serious public health problem. As the sixth leading cause of death in the United States, lung diseases account for more than one hundred thousand deaths each year, forty-six million days lost from work, and forty million days of bed-restricted activities. In addition, pulmonary diseases cost our economy approximately $25 billion annually in lost productivity and wages and added medical care costs.

Although respiratory diseases affect all ages, they are most devastating among the very young and the very old. In the newborn, the most common cause of death is th neonatal Respiratory Distress Syndrome (RDS). Neonatal RDS also is implicated in the development of adult respiratory diseases. Fibrotic and immunologic lung diseases are a major cause of lung problems in the young adult. Respiratory diseases, emphysema, and chronic bronchitis are the major causes of death in young adults and taken together are now the eighth most common cause of death in the United States. An estimated eight million Americans are currently affected by these two diseases, alone. As a disabling disease, emphysema is the third leading cause of worker retirement on worker Social Security disability payments. An additional six million Americans suffer from asthma. It was only twelve years ago that the research mandate of the Institute was expanded to include the lung and that a concerted strategy to meet this very serious health problem was initiated.

We are pleased to report the the NHLBI has worked quickly and effectively in developing plans that are now represented in the National Heart, Blood Vessel, Lung, and Blood Program. This Institute has been at the forefront of the biomedical research community's basic research effort to augment existing knowledge about the structure and function of the lung. To this end, the American College of Chest Physicians enthusiastically endorses the NHLBI's support of research projects regarding: the mechanisms of lung tissue damage and repair; the development of methods to separate major lung cells to determine the ultrastructural and biochemical characteristics of individual lung cells; the role of chemical, mechanical, and neural mechanisms in the control of ventilation; and pulmonary vascular diseases, including pulmonary emboli. The Institute also has innovatively targeted essential research at chronic bronchitis and emphysema, fibrotic and immunologic lung diseases, and respiratory failure.

We are equally excided by the Institute's clinical activities, such as the pulmonary Specialized Centers of Research, and manpower development programs, such as the Pulmonary Academic Awards Program. The Institute's concerted strategy coupled with application of research results in the form of prevention, education, and control programs give cause for optimism to alleviating many caridopulmonary problems during the next decade.

With several amendments, we believe that the "Biomedical Research Training, and Medical Library Assistance Amendments of 1983" would greatly enhance the Institute in this objective, and we request that the Subcommittee give our recommendations its most serious consideration.

Reauthorization of the NHLBI

In order for Americans to reap the full benefits from this initiative, the Institute must be reauthorized for sufficient time to allow for national planning, implementation, and evaluation. Biomedical research projects, training grants, and clinical trials are primarily long-term programs. The one-year and two-year renewals that characterized the reauthorization process during the 1970s greatly hindered the task of planning these long-range activities.

To be accomplished meaningfully, the reauthorization periods should be sufficiently lengthy so that NIH programs can be effectively evaluated. We are also concerned that, given the scant increases in NHLBI funding during the past few years, a short-term renewal will further exacerbate the NHLBI's difficulty in recruiting and retaining highly qualified research manpower.

Accordingly, we support section 102 of S. 773 which extends the legal operating authorities of the National Heart, Lung, and Blood Institute as well as the programs of the other NIH Institutes for three years. We believe that a three-year extension of the NHLBI's programs is essential not only for the Institute to effectively conduct its biomedical research and prevention, education, and control programs, but more importantly, as indicative of Congress' unrelenting commitment to search for new ways to prevent, detect, and control cardiopulmonary and cardiovascular diseases.

ACCP recommends as well that NHLBI's authorization be extended without specific funding authorization levels, so that appropriations can be provided purely on the basis of scientific merit. This legislation represents a laudable attempt by your Subcommittee to make the various NIH authorities consistent with one another. There is no sound reason for funding NHLBI and NCI under specific authorities and the remainder of NIH under Section 301 of the Public Health Service Act. An authorization of "such sums as may be necessary" would provide flexibility for the funding of NHLBI programs in a manner which balances existing scientific opportunities and available fiscal resources.

Should the Subcommittee decide to specify funding authorization levels, these levels should be sufficiently high to prevent further erosion of the Institute's budget and to allow for new initiatives in promising program areas. S. 773 authorizes no increase in appropriations for NHLBI over the FY 1983 level of $622.7 million and only a 5% increase for FY 1985 and 1986. Actual appropriations for FY 1983 for NHLBI were

10.1% over FY 1982 levels. Were the Appropriations Committees inclined, as we hope they will be, to recommend similar increases in FY 1984, an authorization of no increase over the FY 1983 level will constrain the Appropriations Committees in their recommendations for adequate funding for NHLBI and other institutes. Therefore, ACCP recommends that the authorization levels provided in H.R. 1555 be increased to the following levels:

FY 1984 --	$659 million for research and $54 million for Prevention, Education, and Control.
FY 1985 --	$756 million for research and $62 million for Prevention, Education, and Control.
FY 1986 --	$865 million for research and $71 million for Prevention, Education, and Control.

Research funding levels of the National Heart, Lung, and Blood Institute are perilously low. Under the Administration's FY 1984 budget, the NHLBI would fund only about 24% of its approved research grants. The Institute would fund no new clinical trials, no new training starts, and no new manpower development programs. And, because by statute the Division of Lung Diseases receives only 15% of the Institute's overall funds, it is important to maintain sufficiently high overall

NHLBI authorization to assure adequate growth in pulmonary research.

National Research Service Awards

Congress has in recent years made a number of improvements in the Nation's principal biomedical research mechanism, the National Research Service Awards (NRSA) program, including easing the tax burden of trainees and eliminating the payback requirement for the first year of service.

However, the bottom line for the success of the NRSA program is still full-time equivalent trainee support. The Administration's proprosed FY 1984 budget would result in a 10% reduction in the number of young promising investigators who participated in the program. This would exacerbate an already disturbing trend, and it would transmit a loud and clear message to future researchers that the Federal government is unwilling to support the young clinical investigator.

We recommend that the funding authorization levels in S. 773 be increased to $205 million in FY 1984, $235 million in FY 1985, and $265 million in FY 1986. This would insure modest growth in the number of trainees and the stipends afforded trainees.

ACCP supports Sec. 201 which repeals the payback requirement for National Research Service Awards. This will further minimize the disincentives facing the young M.D. facing a decision whether to undertake a research career.

Role of Advisory Councils

Sections 101(d) and 102(d) would provide for Advisory Council approval of all contracts exceeding $500,000 which are supported by the National Heart, Lung, and Blood Institute as well as for the National Cancer Institute. Currently, this Council recommends to the Secretary areas which are appropriate for contract support and the percentage of the Institute budget which could be expended for contracts. We believe that there is a place for advisory council oversight of contracts, but that review should occur in the early stages of the contract process and should be confined to review for scientific merit.

CONCLUSION

Mr. Chairman and distinguished members of this Subcommittee, we applaud you for continuing to demonstrate your commitment to the National Heart, Lung, and Blood Institute and to the national program to combat cardiovascular, pulmonary, and blood disorders. In sum, we urge that you provide for a three-year authorization for the National Heart, Lung, and Blood Institute and the National Research Service Awards program, and that you adopt our recommendations regarding the funding of the Institute; its Prevention, Education and Controls program; and the role of the National Heart, Lung, and Blood Advisory Council.

In the spirit of mutual cooperation and support, it is our hope that you will continue to call upon us for advice and consultation whenever you think we can be helpful to you and the Subcommittee.

Thank you.

RESPONSES OF DR. TALBOT TO QUESTIONS FROM SENATOR HATCH

1. "Could you explain why core grants are necessary for productive research at your facility?"

I have attempted to answer this question in a way that goes beyond our own facility at Fox Chase, because there are approximately 63 centers, of considerable diversity, all of whom depend upon core grants with somewhat different emphasis on the separate components of their core grants.

To state the central points: core grants have made centers possible and have made them function. They have provided for "centerness;" for space in some cases; for shared equipment; have enhanced collegiality; have cemented staff together in a common purpose; have optimized interdisciplinary communication for both creativity and quick exploitation of new leads; and have been a major reason for the development of a network of centers where high quality creative work has emerged that has been funded in the competitive market of peer review processes. As we have often said, these grants are "the glue that holds the centers together."

Why are these core grants so important? It is not simply a matter of having more money. It is, instead, because of the ways in which that money is made available and how it can be used. The money that is supplied by core grants to centers is especially important because of the mechanism and form in which it comes to the centers.

If it is decided to reduce or obliterate core grants, and if as a result more R-01's and P-01's are thus made available, then in some fashion that amount of money will need to be found to replace what was removed from the centers--it is also true that this "replacement" will, to the extent possible, be found from R-01 or P-01 grants. But the only places that would be victims of "taking from" would be the centers.

Modern biomedical research requires an institutional and organizational support system that is far different from the casual laisez-faire processes of the past. Core grants provide this essential infrastructure, cohesiveness and purpose without which our quality would be certain to suffer. A collection of individual R-01 and P-01 grants simply cannot, alone, qualify as an institution that is designed for stability and vibrancy.

2. "In your opinion, why have the overall statistics for cancer prevalence and deaths from cancer, not improved more than they have over the past decade, given the great amount of money spent on research?"

The question refers to "overall statistics." In order to answer the question in a meaningful way, we need to consider the data for each of the many types of cancer.

First, we can safely say that we do not know the cause, or a major cause, of most cancers--but even if we consider this group of cancers, it is possible to state that there have been many significant improvements in the success of treatment. As Dr. Vincent DeVita described in his testimony before this committee and in his written statement supplied to the committee, there are some striking examples of progress. He referred to the decrease in mortality rate for Americans under the age of 45; and to the fact that "fully 46% of patients with the serious cancers survive their disease 5 years and many of them are cured."

Dr. DeVita then gave the following statements:

- "For ovarian cancer, the national mortality rate fell 38 percent because of better staging of patients and wiser application of existing chemotherapy and radiotherapy;
- For premenopausal women with breast cancer, a 15 percent decline is attributable to the application of adjuvant chemotherapy;
- For testicular cancer, a 43 percent decline is the result of new drug therapy introduced in 1976. That advance, along with the radiation used as standard treatment for one form of the disease, makes testicular cancer curable in most cases--even when diagnosed in the most advanced stages;
- For Hodgkin's disease, a 56 percent decline in the mortality rate, and for other lymphomas, a 29 percent decline, are due to combination chemotherapy; and
- For bone cancer, a 19 percent decline is because of overall better application of surgery, radiation therapy and cancer chemotherapy in these patients.

These decreases in mortality related to treatment advances took a minimum of 5 and most often 10 years to occur on a nationwide basis because of slow diffusion of new information to physicians not trained in cancer management. It is this gap we hope to reduce to one year this summer with the completion of the PDQ system."

In addition, cancer of the stomach has greatly diminished, perhaps because of some way in which our food processing or our diets have changed during the last 30 or 40 years.

These are at least examples of progress in this group of cancers.

A second group of cancers includes those for which we do know either the cause or the major cause. As we all know this includes lung cancer. It also includes a proportion of bladder cancer. To some degree, at least, it includes many skin cancers. It appears also to include cancer of the larynx, nose and throat, possibly esophagus. It now is also possible to state that it includes primary cancer of the liver.

Of the cancers referred to above:

- Bladder cancer has been greatly reduced in incidence by the application of industrial health measures, by improved methods of screening high risk patients, by improved diagnosis and staging, and by improved therapy.

- We all know the story about lung cancer--not only in men but increasingly in women. This is an issue that the NCI, or centers, cannot solve alone. This is a public health issue. An issue that communities, schools, businesses corporations and states--to name a few--must address. We can help a little, but not much as long as the state and other departments of health remain passive. Let me give you an example: We at Fox Chase Cancer Center have worked for many years in an effort to establish a tax in Pennsylvania on cigarettes, to help fund "The Pennsylvania Cancer Control, Prevention and Research Act." The act has passed and is in effect--but the funding is borderline and in jeopardy. Perhaps some Federal-State partnership could be useful here; but we all despair that this will be difficult.

- Smoking cigarettes is also a factor in other cancers, including larynx, mouth, nasal passages--perhaps others as well.

- Primary cancer of the liver is one of, if not the, most common cancers in some parts of the world, especially Asia and Africa. It is now known to be associated with chronic infection with the hepatitis B virus. As you are aware, a vaccine has been developed by Dr. Baruch Blumberg of our institution and is now being produced and marketed by Merck.

Thus, we have another situation in which the cause is known (at least, the major cause); the prevention is known; and the solution now rests with public health measures and organizations--not with the NCI. The NCI, and at times, other NIH institutes, supported the work that led to this accomplishment, but now public health processes must take over.

- Skin cancers and exposure to sunlight--here again, we are dealing with lifestyle and public health measures including education. The NCI has done as much as it can, I believe--and once again other agencies must help.

The above statements, I hope, offer optimism in some cases; success available in others; and some pessimism about human lifestyles and behavior in others. But even in the latter cases, I believe that we will someday learn how to teach young people not to smoke! After all, Dr. DeVita said that there is an 18 percent decline in mortality from lung cancer in men, attributable to smoking cessation campaigns. So that is an impressive beginning in a difficult area.

3. "In your opinion, do the various cancer centers throughout the country devote an appropriate share of their resources to research in cancer prevention?"

The answer is an unqualified "yes!" Obviously, we never move as fast as we all wish--but huge progress is already being made in this area.

It is especially important to realize that all creative high quality biomedical research has the potential of providing genuinely useful methods of prevention. It is my personal view that "targeted" or "designed" research in prevention is very difficult to design and is rarely as productive as that which the great exciting mass of exploding biomedical and biological knowledge is likely to produce.

Cancer centers have, as noted above, competed for peer reviewed grants with outstanding success. The new centers achieved excellence with remarkable rapidity and the relatively new ones continued to develop and improve. Here, I believe firmly, is the avenue to future knowledge that will lead to a practicable series of preventive measures.

QUESTIONS FOR DR. EPHRAIM ENGLEMAN

1) WE THANK YOU FOR COMING ALL THE WAY FROM CALIFORNIA TO TESTIFY FOR THE HEARING TODAY. AS YOU KNOW, I AM SYMPATHETIC WITH THE NEED FOR IMPROVED ARTHRITIS RESEARCH AND APPRECIATE YOUR EXCELLENT TESTIMONY. IN SPITE OF MY ENTHUSIASTIC SUPPORT FOR CREATION OF A NEW NATIONAL INSTITUTE OF ARTHRITIS, MUSCULOSKELETAL AND SKIN DISEASES, I AM CONCERNED ABOUT THE QUESTIONS RAISED BY DR. BRANDT REGARDING ADMINISTRATIVE COSTS AND THE POTENTIAL FOR MANY NEW PROPOSALS FOR SEPARATE INSTITUTES. IN YOUR OPINION, WHAT WOULD BE THE COSTS OF ADMINISTRATING THIS NEW INSTITUTE? IN YOUR OPINION, WOULD FURTHER NEW INSTITUTES BE APPROPRIATE AT NIH?

2) AS I UNDERSTAND IT, ARTHRITIS IS ACTUALLY MANY DISEASES MANIFESTING THEMSELVES IN SEVERAL DIFFERENT WAYS. A GREAT DEAL OF RESEARCH HAS BEEN CONDUCTED IN THE PAST, MUCH OF IT DEVOTED TO FINDING DRUGS WHICH WOULD PROVIDE RELIEF FROM PAIN AND HOPEFULLY DISABILITY. HOWEVER, IT SEEMS TO ME INSUFFICIENT RESEARCH HAS BEEN CONDUCTED IN THE PREVENTION OF THESE DISORDERS. WHAT IS YOUR OPINION ABOUT RESEARCH IN THE PREVENTION OF ARTHRITIS, AND DO YOU BELIEVE THERE IS POTENTIAL FOR ACTUALLY FINDING CURES FOR THESE DISORDERS IN THE NEAR FUTURE?

**THE
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RESPONSES OF EPHRAIM P. ENGLEMAN, M.D. ON BEHALF OF THE ARTHRITIS FOUNDATION WITH RESPECT TO QUESTIONS FROM SENATOR HATCH ON S.773

1. The Arthritis Foundation believes that the NIH estimate of the new costs of administering a National Institute of Arthritis and Musculoskeletal Diseases is grossly inflated. Although NIH has been requested to supply its methodology for determining the increased cost, along with a detailed breakdown of the cost estimate, this has not been forthcoming.

Based upon our knowledge of the management and administration of NIADDK, and of Federal agencies generally, it is our firm belief that a maximum additional $1.1 million would be required to make the new institute fully operational as a free-standing, separate entity. Some $3 million are already identified by NIH as administrative costs attributable to the Division of Arthritis and Musculoskeletal and Skin Diseases in NIADDK. There is no valid reason why the personnel, salaries and expenses, equipment and facilities identified with the Division, along with an appropriate percentage of the NIADDK overhead, could not be "spun off" from the parent institute.

As to the second part of your first question, we are unable to recommend policy on adding NIH research institutes beyond the proposed arthritis institute. We believe we have made a strong case for the establishment of a discrete arthritis institute. There is no optimum number of research institutes, nor an immutable ceiling beyond which no new institute should be created. There was institutional opposition to the creation of the Aging and Eye

Institutes, and arguments similar to those now being made were raised then. But both institutes have enhanced the mission of, and brought credit to, American biomedical research and NIH. We fully expect that an arthritis institute would do the same.

2. I agree that there has been insufficient research in the prevention of arthritis. In fact, virtually no work in this area has been done. It is of course reasonable to assume that prevention will be easier when we have identified the cause. Indeed, the predominant thrust of our research programs has been toward the discovery of causes and mechanisms. Important investigations in genetics, immunology, virology and other biomedical disciplines have in fact resulted in major advances in our understanding of these mechanisms. For example, immunogenetic investigations have demonstrated the presence in patients of blood markers which indicate predisposition to certain types of arthritis. If the specific triggering factor in a given type of arthritis turns out to be infectious, a vaccine against that infectious agent could prevent arthritis in the predisposed individual.

Research in prevention need not and should not await discovery of the cause. Epidemiologic studies in the past have identified risk factors of certain diseases prior to detailed understanding of their causes and have contributed significantly to their prevention. Such studies have pinpointed the definite relationship between cigarette smoking and the development of lung cancer and emphysema, the risk factors of high blood pressure, smoking high levels of blood cholesterol in the development of heart disease. Epidemiology--by definition--the study of the distribution, the natural history, and the determinants of human disease--is a scientific discipline which can fill many of the gaps in our current knowledge about arthritis. Epidemiologic research in arthritis, grossly neglected because of lack of funds, requires long term, stable support. It would and should complement bench and clinical research in future efforts to identify not only the cause and cure of arthritis but also methods of prevention.

Is there potential for actually curing these disorders in the near future? There has never been a more propitious time. However, the magnitude of the problem and the existing opportunities dictate the need for new national leadership, greater flexibility and visibility which only a National Institute of Arthritis and Musculoskeletal Diseases will provide.

The CHAIRMAN. The committee now stands in recess.

[Whereupon, at 11:50 a.m., the committee recessed, to reconvene at the call of the Chair.]

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